VOLUME 33 AUGUST 1940 NUMBER 8

Southern Medical Journal

Journal of the Southern Medical Association

Copyright, Southern Medical Association, 1940. Published monthly by the Southern Medical Association, Empire Building, Birmingham, Alabama. Annual subscription, $4.00. Entered as Second-Class Matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, November 12-15, 1940

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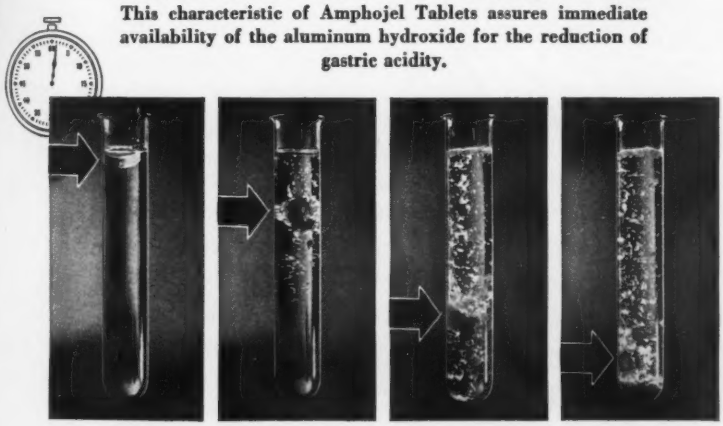

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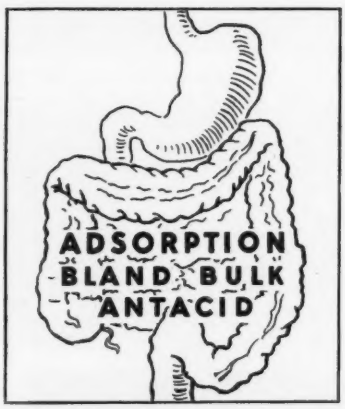

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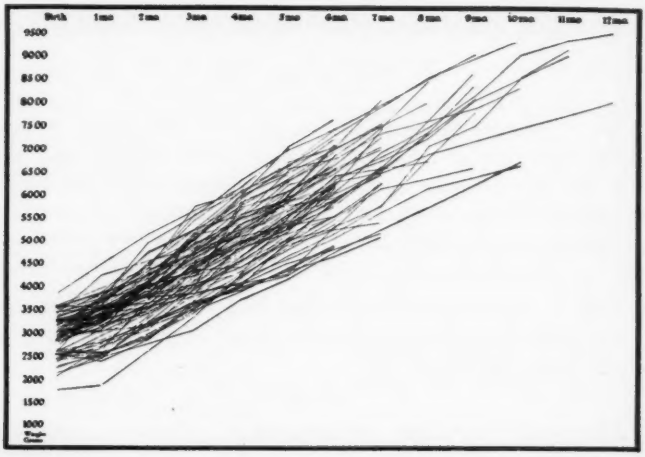

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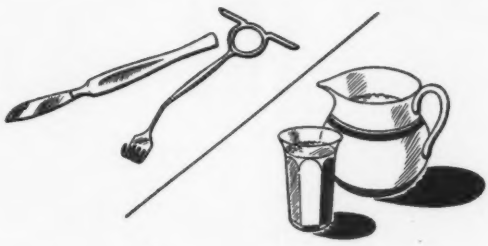

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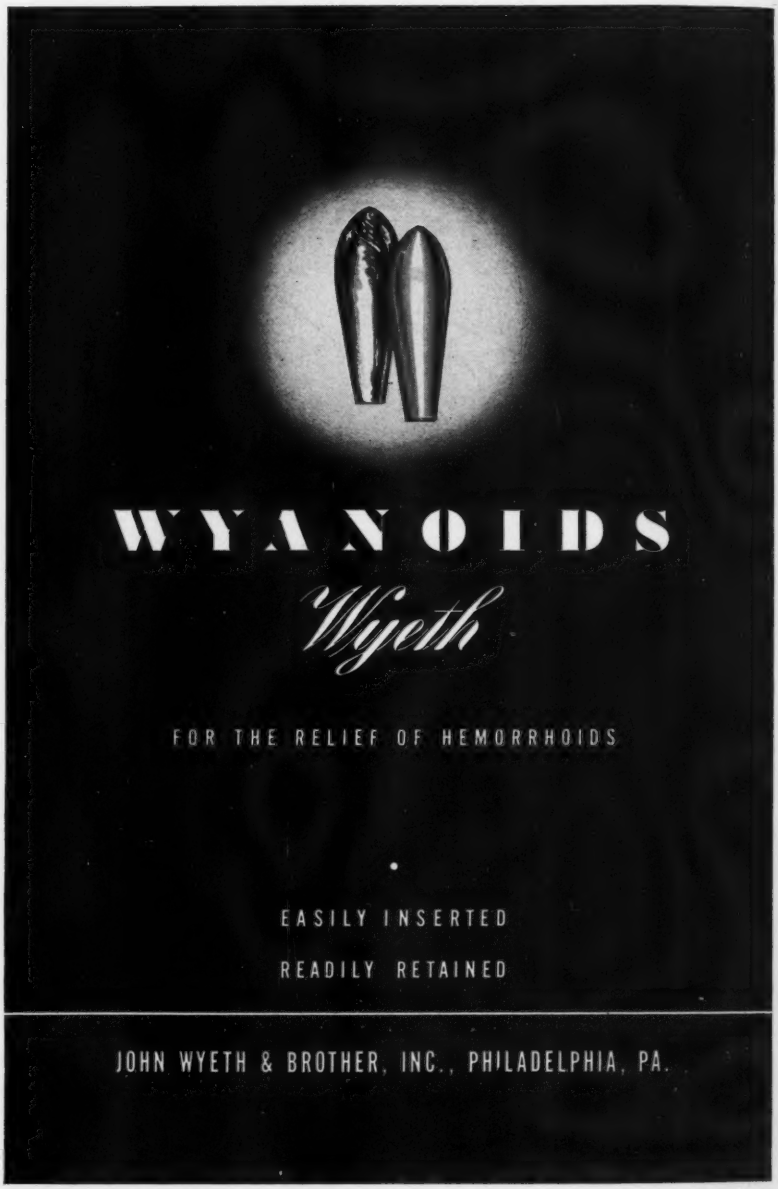
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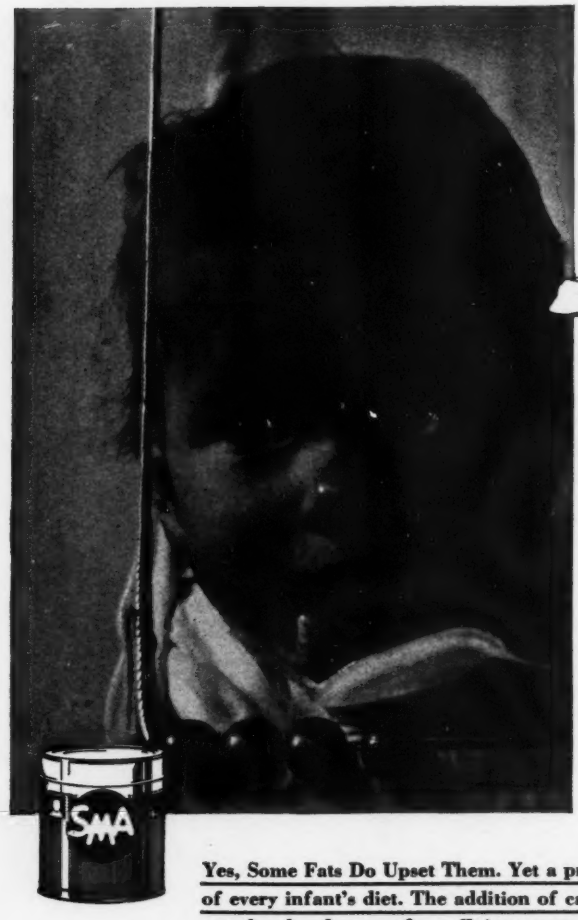

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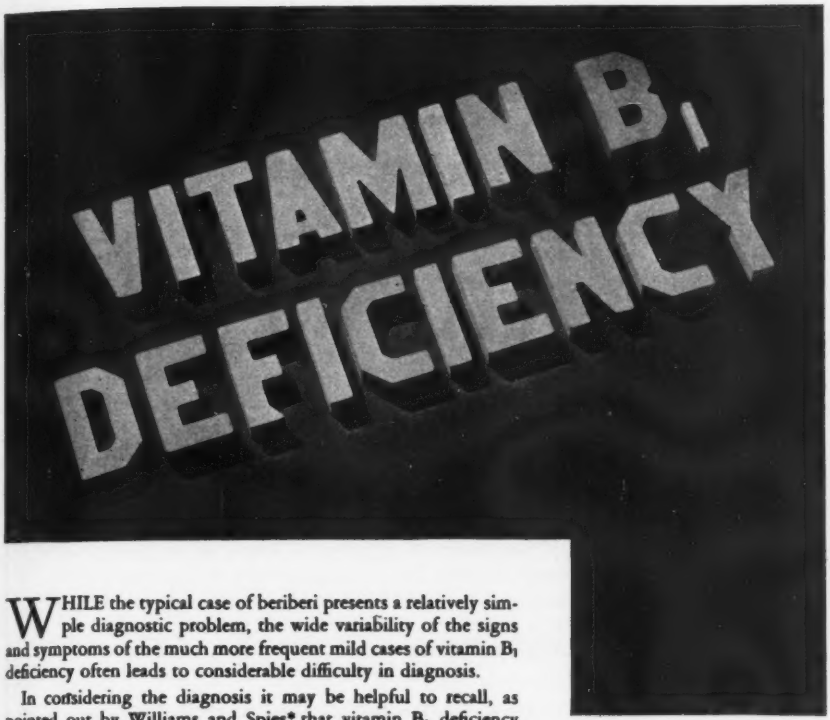

WHILE the typical case of beriberi presents a relatively simple diagnostic problem, the wide variability of the signs and symptoms of the much more frequent mild cases of vitamin B_1 deficiency often leads to considerable difficulty in diagnosis.

In considering the diagnosis it may be helpful to recall, as pointed out by Williams and Spies,* that vitamin B_1 deficiency occurs especially among the following groups:

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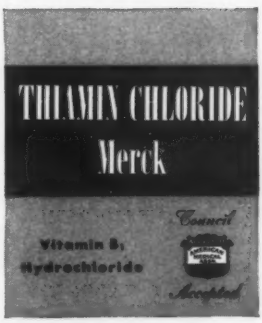
In cases of vitamin B_1 deficiency, the daily administration of adequate amounts of thiamin chloride will ensure a prompt therapeutic response. When absorption from the gastro-intestinal tract is impaired, parenteral administration of thiamin chloride is indicated.

Literature on Request

*Williams, R. R., and Spies, T. D., Vitamin B_1 and its use in medicine, The Macmillan Co., New York, 1938.



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* **"PEPTIC ULCER**—The Effect of High Protein Diet on the Behavior of the Disease" by Windwer and Matzner, Am. Jl. Dig. Dis. 5:743, 1939.

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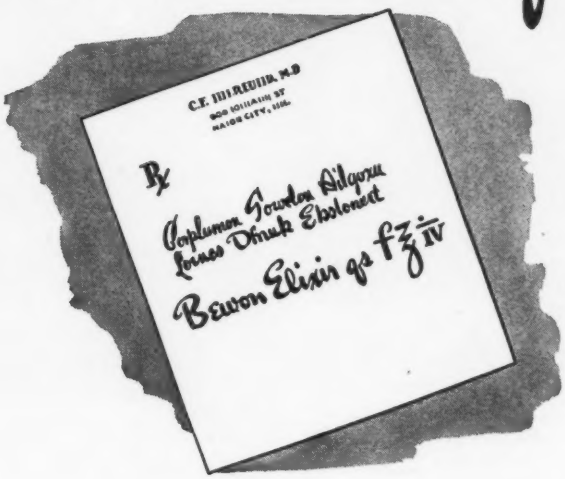

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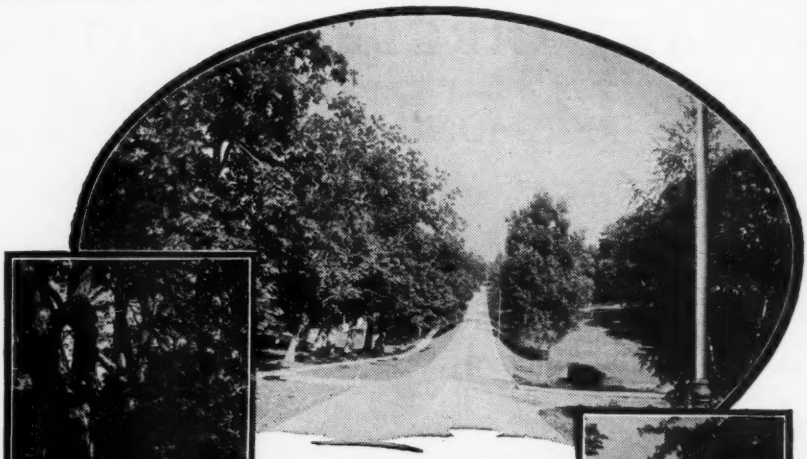

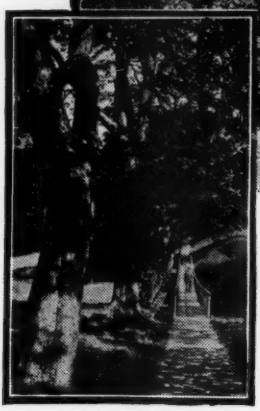

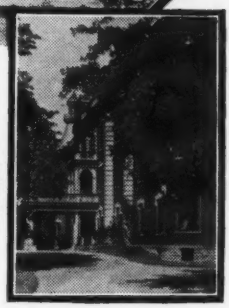

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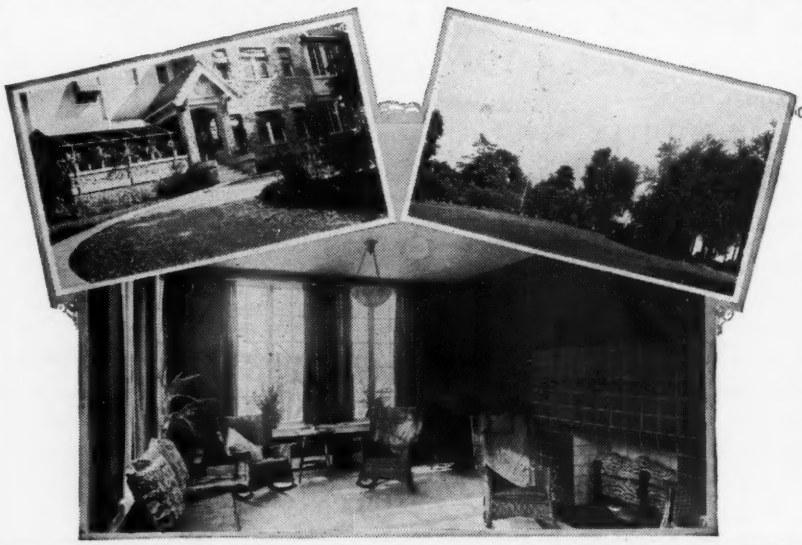

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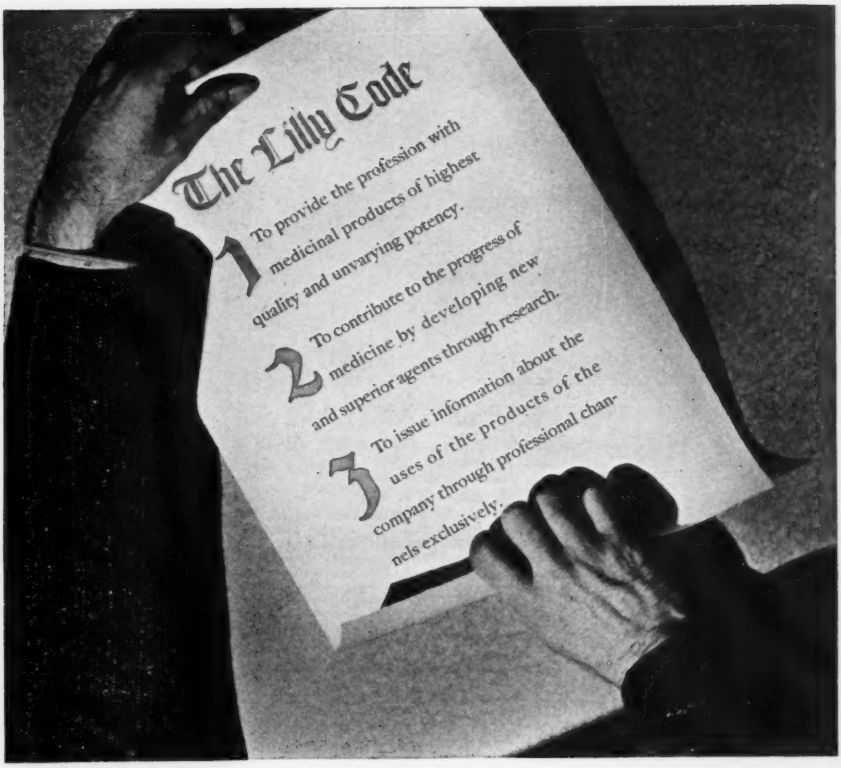
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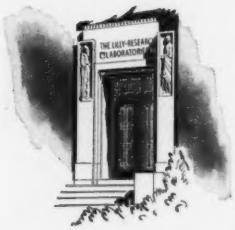

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JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

PUBLISHED MONTHLY BY THE SOUTHERN MEDICAL ASSOCIATION AT BIRMINGHAM, ALA.

Volume 33 AUGUST 1940 Number 8

CHRONIC BACK PAIN WITH SCIATICA*

By LAWSON THORNTON, M.D.
and
CALVIN SANDISON, M.D.
Atlanta, Georgia

Probably the lumbosacral junction is subjected to greater strains than any other part of the body. Many structures such as bones, ligaments, fascia, muscles, tendons, cartilages and nerves become vulnerable under the forces to which they are subjected. It would be wrong to assume that any of these structures is the only vulnerable one. Instead each should be considered a possibly damaged structure in every low back problem. By careful study, using every diagnostic aid, localization can now be worked out with much accuracy. In addition to instruments of precision, clinical experience is still essential in order to discriminate between important and negligible findings.

Strange as it seems, the origin of pain is not always where it hurts. We find it difficult to convince patients that pain in a knee is the symptom of disease in a hip, or that there is such a thing as referred pain along the sciatic nerve without direct sciatic nerve involvement. It is just as difficult to convince ourselves of the fact that abnormal reflexes and areas of disturbed anesthesia are not positive proof of nerve or cord compression.

As the result of the work of Drs. Barr and Mixter we are indeed grateful that we can now distinguish between a real intraspinal condition and one referred from some other structure outside the spinal canal.

Diagnostic unraveling of low back pain makes an interesting study. In working out this problem there has always been that variable quality to fall back upon, namely, the so-called personal equation. The less we concerned ourselves with the intricacies of anatomical mechanics the simpler the problem seemed. There was a time when the whole syndrome was just lumbago, sometimes accompanied by sciatica and sometimes not. Treatment was as simple as diagnosis and successful in a remarkably high percentage of cases.

As time passed on, various schools of thought developed. Each believed it had found the seat of the trouble and devised a remedy, based by some on clinical facts and by others on theory only. Regardless of the various plans the results were relatively satisfactory. Each enthusiast sincerely believed his plan to be correct and his results seemed to justify the belief. But, on re-examination and follow-up, none of the series of cases is as good as one would like it to be. And, too, time and natural healing have not been given the share of honor they deserve. So it would seem there must be many causes of backache, requiring different lines of care and some recover without any treatment at all. Failure and recurrences may be expected if one follows any one single school, but with more accurate consideration of all possibilities, a higher percentage of good results certainly might be anticipated.

It is our opinion that as a general rule one should be conservative in all recent cases and that surgery should be considered only when enough time has elapsed to prove the condition to be persistent and chronic.

In the presence of sciatica it is not enough for the surgeon to fall back on the surgical procedures practiced in the past without first making the intraspinal study. If he disregards the possibility of obstruction within the canal and performs a sacro-iliac or lumbosacral fusion, he will have a high percentage of satisfactory results, but he will occasionally overlook a ruptured disk or hypertrophied ligamentum flavum.

*Read in Section on Railway Surgery, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

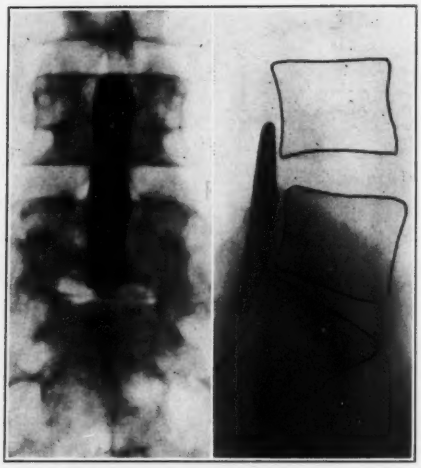

Fig. 1

X-ray of intraspinal iodized oil as it appears in the normal spine. Anteroposterior and lateral views. This man of 32 years had backache and sciatica of two years' duration. Relieved by operation for fusion of lumbosacral joint.

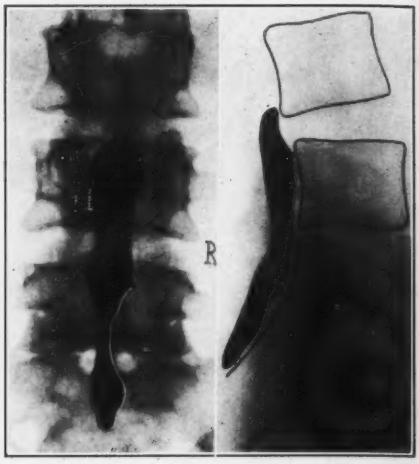

Fig. 3

Demonstrating a defect in the column of iodized oil on right side opposite lumbosacral junction of spine. This was a man of 34 years with lumbosacral pain and right sciatica for 16 months. Lateral x-ray shows this is not a ruptured intervertebral disk. At operation (hemilaminectomy) a thickened ligamentum flavum was found partially constricting spinal canal and lumbar 4 nerve root. Man relieved of pain and has returned to regular work. (See Fig. 8.)

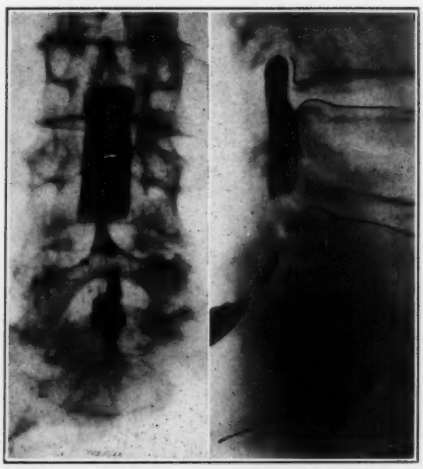

Fig. 2

X-ray of spine immediately after injection of iodized oil. In fluoroscope the oil almost completely "blocked" at the level between lumbar 4 and lumbar 5, and trickled through slowly a drop at a time. The obstruction was caused by an extradural rupture of intervertebral disk. The chronic backache and sciatica have been relieved entirely following our removal of the protruding disk. (See Figs. 5 and 6.)

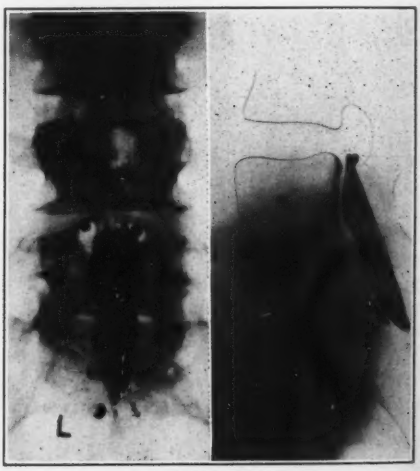

Fig. 4

From x-ray fluoroscopic study following intraspinal injection of iodized oil in this man with low backache and sciatica it was apparent in lateral view that there was a posterior protrusion of lumbar 5 intervertebral disk. A hemilaminectomy was done. The protrusion was found to be smooth, entirely midline and with no evidence of nerve root compression. It was our opinion that the protrusion was not the cause of sciatica and lumbosacral fusion was done (Fig. 10). The man has been relieved of his sciatica and also the pain in his back.

Nor is it enough for the surgeon, having found neurologic changes and a "defect" by means of the study with iodized oil, to plan for exploration of the canal and removal of what he considers the cause of pain. In this case he will also have a high percentage of satisfactory results, but some failures, having overlooked indications for spine fusion.

It becomes evident that a single method applied in all cases of chronic low back pain with sciatica is unreliable. Benefits come from each, and the best results will be obtained from a refined judgment of what procedure to follow after the canal has been explored, and not before.

When the study with iodized oil is negative, the spinal canal is considered normal and the surgeon may proceed with spine fusion. When large defects are present in the studies with iodized oil, as seen in both anterior-posterior and lateral views, they are diagnostic of protrusion of tissue within the spinal canal and removal of these protrusions would be expected to give relief. Often defects are found that we consider to be within normal limits, or border line. Just

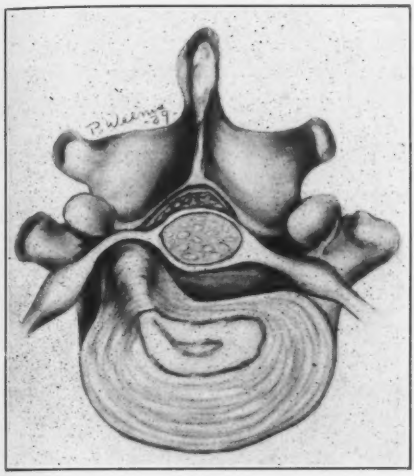

Fig. 5

Drawing to illustrate rupture of intervertebral disk with pressure against nerve root. Recent analysis of statistics at one of the largest clinics show that 3 per cent of all low back conditions with sciatica are caused by intervertebral disk protrusion.

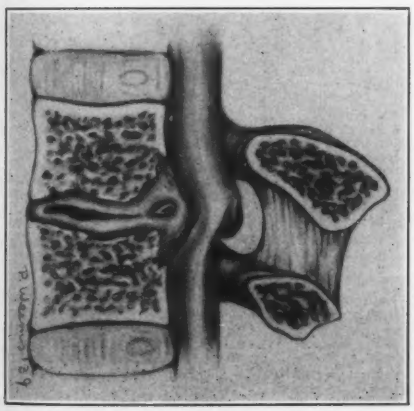

Fig. 6

Drawing of ruptured intervertebral disk, lateral view. (See Fig. 2.)

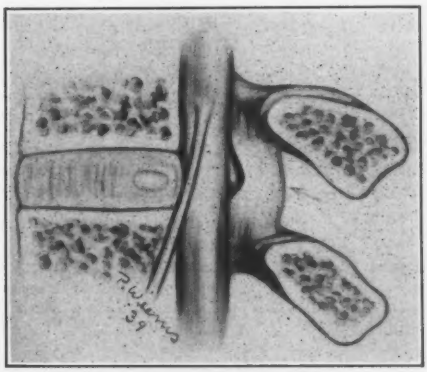

Fig. 7

Drawing of normal relations of ligamentum flavum to spinal cord and nerve root. This ligament spans the opening between the posterior arches of the vertebrae and together with the laminae forms the posterior wall of spinal canal.

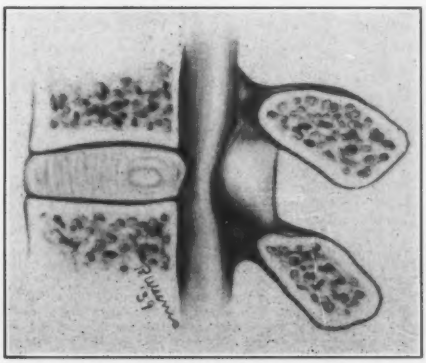

Fig. 8

Ligamentum flavum, thickened and pressing on dura. (See Fig. 3.)

as in all x-ray interpretations, there is danger of seeing erroneously what one is looking for. Normal irregularities and slight anomalies are to be discounted.

If the defects with opaque media suggest a protrusion within the canal, bordering between the normal and a definitely harmful one, the disk region can be explored at the time of operation. With a visible and palpable nerve root compression, or swelling or cord compression, the protrusion should be removed; otherwise it should be disregarded and a spine fusion performed. In cases where harmless protrusions have been removed and the patient is relieved of pain, credit must go to the surgery done outside the spinal canal and not to that done within.

Some time ago we realized the necessity of formulating a routine procedure for working out these problems and the evolved plan is about as follows:

First the patient's story tells of the severity of the pain, its acuteness or chronicity, the resulting disability and just what conservative treatment has been given. After careful study, a decision is made whether further conservative treatment is to be carried out or surgery undertaken. The plan is explained in detail to the patient. This is important in order to have his entire cooperation in completing the study. If surgery is decided upon he is admitted to the hospital a day or two before operation, and soon after admission an intraspinal x-ray study with iodized oil is made. If this examination shows what may be interpreted to be a protrusion causing spinal cord pressure, a hemilaminectomy and removal are planned.

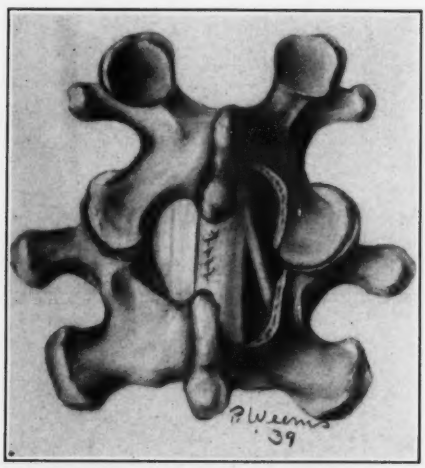

Fig. 9

Drawing of hemilaminectomy for removal either of ruptured intervertebral disk or thickened ligamentum flavum. On the left side the ligamentum flavum has not been removed and covers that side of spinal cord. On the right the ligament has been removed together with part of lamina above and below in order to give adequate exposure to dura and nerve root.

SUMMARY

There are many causes of backache and sciatica and there are also different plans of treatment, each plan successful in many cases.

Recovery without treatment is not unusual.

Conservative treatment is almost always indicated in recent cases.

Chronic cases may require surgery.

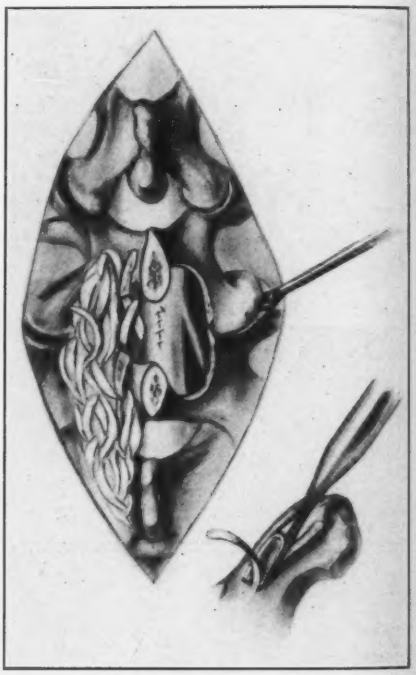

Fig. 10

The plan of spine fusion done at the time of hemilaminectomy is becoming more generally accepted. It is the plan we follow at the time of removal of intervertebral disk. Its purpose is to immobilize permanently a damaged anterior wall of spinal canal at site of rupture, and to prevent recurrence. Drawing shows hemilaminectomy with spine fusion. It also shows curette in facet for removal of cartilage. Multiple small bone grafts are taken from laminae and spinous processes. Inset: Detail of curling a bone graft from side of spinous process.

DISCUSSION (*Abstract*)

Dr. Willis C. Campbell, Memphis, Tenn.—The diagnosis of pathologic conditions of the lumbosacral region has been and still is a puzzling orthopedic problem. I have for a great many years classified lesions of this region as follows: infections, definite traumatic lesions, extraspinal lesions (lesions not associated with the osseous structure of the spine), bony lesions and intraspinal lesions, and have realized that the last is a very definite factor.

Dandy, a number of years ago, first called attention to the occurrence of rupture of the intervertebral disk. In recent years the diagnosis and treatment of this condition have been perfected so that now we have a reasonably definite clinical entity. In all probability, many cases which have failed to respond to orthopedic treatment in the past have been due to rupture of the intervertebral disk.

In conjunction with Drs. Semmes and Murphey (neurological surgeons in this city) we have observed 97 cases of rupture of the intervertebral disk. I have always been opposed to the injection of iodized oil, realizing that any foreign substance remaining in the spinal canal is a possible source of difficulty and may cause medicolegal complications. It is true that in some cases most of the iodized oil can be removed, but its total removal is practically impossible. In our personal experience, no harmful effect has been observed following its use; however, we are aware of the fact that in the literature a few cases have been reported in which subsequent pathological findings were attributed to it.

Iodized oil has been used in 39 cases. Fifty-eight cases have been operated upon without its use. These cases were diagnosed by careful orthopedic and neurologic examinations. In those cases which were injected with iodized oil, a rupture of the disk was diagnosed in four cases in which the disk was not found at operation. Consequently, with this method of diagnosis the percentage of error was 10.4. The percentage of error in those cases operated upon without iodized oil was 8.6. We realize that this is a small series, but in view of the statistics quoted and the possibility of difficulty following the injection of the opaque medium, we have discontinued its use and have preferred to depend on careful physical examination to make the diagnosis.

In doubtful cases, where it is impossible to predict accurately whether the cause of the low back pain is the ruptured intervertebral disk or an osseous lesion of the spine requiring fusion, the following procedure has been adopted:

The operation is carried out jointly by the neurologic surgeon and the orthopedic surgeon. Exploration of the spine for an intervertebral disk is first done by the neurologic surgeon. If a rupture of the intervertebral disk is found, it is removed and no further operative procedure performed. If the neurologic surgeon is unable to find a pathologic condition sufficient to account for the patient's pain, fusion of the spine is done by the orthopedic surgeon, provided the patient's general condition is such that a dual operation of this type is warranted. We have preferred not to fuse patients in whom a rupture of the intervertebral disk was found, as it would be impossible to determine whether the end result following such a procedure were attributable to the removal of the disk or to the fusion of the spine.

This is a most interesting subject to railroad surgeons on account of the compensation factors. I feel certain that many of these cases, particularly in the early stages, even though they show symptoms of a disk, can be treated conservatively. A reasonable period of conservative treatment is indicated before operative measures are undertaken. I believe that this is also Dr. Semmes' opinion.

Spinal lesions are exceedingly numerous and we have been treating them for many years. It is true that failure has resulted in many cases. On the other hand, we must remember that a large proportion of these cases has been successfully treated. The proper management of cases with rupture of the intervertebral disk should improve our total percentage of good results.

Dr. R. Glen Spurling, Louisville, Ky.—Dr. Thornton and Dr. Sandison have introduced a very important subject here this morning, probably the livest one in the field of orthopedic and neurological surgery today.

I want to endorse heartily what Dr. Campbell said about the necessity for conservative treatment in the acute stages of low back and sciatic disturbance. In our opinion, operative intervention should be reserved for those patients who have failed to respond to adequate conservative measures.

The use of iodized oil for diagnosis is the most controversial feature of the whole problem. One cannot simply inject iodized oil and expect it to go through the x-ray diagnostic machine and get a satisfactory interpretation. No roentgenologist, no matter how experienced, can consistently rely upon his interpretations without considering and correlating the clinical findings presented to him by the neurologist. We look upon iodized oil now as being a localizing medium rather than a diagnostic one. We feel that the diagnosis should be made on clinical findings and when iodized oil is necessary it should be used only for accurate localization of the lesion.

From our experiences during the past year we feel that approximately 50 per cent of all cases needing surgery can be diagnosed and localized on clinical findings alone.

What are the neurologic findings in ruptured intervertebral disk with herniation of the nucleus pulposus?

The symptoms as presented by an observing patient may be so characteristic that the proper diagnosis and even the localization of the lesion may be prophesied with accuracy from the story alone. There have usually been recurrent attacks of lumbago before the sciatic pain appears. However, many patients have the sciatic pain during the initial attack of lumbago. At any rate, almost invariably the back pain precedes the sciatic pain. The points of greatest pain are usually in the back, hip, back of the thigh, or in the knee. Some patients have pain on the lateral aspect of the leg and foot. There is usually intensification of pain on coughing, straining, and sneezing. Bending forward usually intensifies the pain in the back and leg. Patients usually get no relief from lying down. Many of them are more comfortable sitting or standing. When the leg pain is prominent they usually complain of numbness or tingling sensations in the lateral aspect of the calf or leg or the foot.

How can these symptoms be correlated with a rupture of the intervertebral disk?

We believe that the back pain is produced by tearing of the annulus fibrosus and stimulation of the nerve endings in the structure, and that the leg pain is pro-

duced only when the nucleus pulposus or a piece of the fragmented annulus fibrosus is extended into the spinal canal, thus compressing one or more roots of the cauda equina.

On clinical examination the following signs are usually present in the intractable case:

(1) There is a stiff lumbar spine and normal lumbar curve is obliterated. Bending forward intensifies the pain in the back and in the leg. Bending lateralward, especially toward the affected side, intensifies the pain.

(2) The leg raising test of Lasegue is always positive in those cases with sciatic pain. This test is performed by flexing the thigh on the trunk and extending the leg until pain appears. Then suddenly dorsiflexing the foot intensifies the pain in the sciatic distribution.

(3) Careful sensory examination of the affected leg with pin prick, hot and cold test tubes of water and cotton usually demonstrates a sensory loss in the fifth lumbar or first and second sacral dermatomes. You will recall that the fifth lumbar dermatome includes the great toe and a narrow strip over the skin. The first sacral dermatome includes the anterior part of the lateral aspect of the leg, the top of the foot, and the dorsal surface of all the toes except the great toe. The second sacral dermatome is over the posterolateral aspect of the calf and the back of the thigh.

(4) With herniations at the fifth lumbar interspace the Achilles jerk is usually reduced or absent. With herniation at the fourth lumbar interspace, the Achilles jerk is usually unaffected. The knee jerks are unaffected unless the herniation occurs at the third lumbar interspace.

(5) Compression of the jugular veins, thus increasing the intracranial and intraspinal pressure, may cause intensification of pain and numbness and tingling in the fifth lumbar, first or second sacral dermatomes. This, the so-called Naffziger test, is pathognomonic of an intraspinal lesion.

In closing, I should like to say a word about the technic of operations for removal of these lesions. Only enough bone of the lamina is removed to permit dissection of the ligamentum flavum. The dura and nerve root over the lesion are reflected medially, and the disk is removed without opening the dura or disturbing any of the weight-bearing surfaces of the vertebral column. When it is possible to remove a lesion in this manner we feel that it is superfluous to consider spinal fusion.

Dr. R. Eustace Semmes, Memphis, Tenn.—In our last fifty cases we have used iodized oil in only six cases. In four cases in which no defect was shown with iodized oil, we explored the patients on clinical evidence and found and removed ruptured disks and in each case this cured the patients' symptoms. We have not quite completely abandoned the use of either air or iodized oil, but reserve it for doubtful cases.

I believe the average time that our one hundred operative cases have spent in bed after operation has been seven days, and the average time in the hospital nine days. If this is compared with some of the other procedures, I think you can see why Dr. Campbell and I have come to the conclusion that once a patient has a well established syndrome, particularly as Dr. Spurling pointed out, involving the nerve root, he should be operated upon by hemilaminectomy. Certainly, however, as long as the pain is limited to the back, of short duration, or not disabling, he should have conservative measures first.

Cooperation between the orthopedists and the neurosurgeons is essential in the study of these patients for the protection of both fields.

Dr. Ralph Ghormley, Rochester, Minn.—There is little I can add to what has already been said. I think we at The Mayo Clinic have come more or less to a viewpoint expressed by Dr. Campbell and Dr. Semmes, in which cooperation between orthopedic and neurologic surgeons is essential.

Radiopaque oil now is used much less than formerly for two reasons: first, because we do not like to leave it in the spinal canal; and second, because the results obtained by its use are sometimes misleading. One can have a normal roentgenogram after the injection of radiopaque oil and yet be certain that there is a protruded disk and on exploration find one. I think we are all coming to the conclusion that the clinical examination is by far the most important, and certainly with the problem of the protruded disk before us in the last three or four years, the neurologic examinations have been very helpful in suggesting the presence of protruded disks.

As far as the fusion operation is concerned in combination with the disk, I should say our present standpoint is about as follows: if no disk is found when one is suspected, fusion is indicated. Also, in those cases in which there is some congenital anomaly, such as a break in the pedicles, and, as you know, these are not uncommon in the lumbosacral region, fusion is indicated. Also, if, in spite of complete removal of the disk, symptoms persist and long continued disability and a certain amount of instability of the posterior pedicle ensues, fusion may be indicated.

Certainly within another year or two our viewpoint may be changed, but at least we are all converging on a more or less common ground, and I think now protruded disk is established as a clinical entity, and its proper treatment will be more clearly understood within a few years.

LOW BACK PAIN*

By PAUL C. WILLIAMS, M.D.
Dallas, Texas

The knowledge which has been gained during the past fifteen years regarding the condition spoken of as low back pain, lumbago and sciatica if properly correlated should practically eliminate the confusion which has been associated with these conditions. The literature of the past decade has presented many theories which to those who do not specialize on this ailment may appear to be severely contradictive. It is the opinion of the author that this is not the

*Read in Section on Radiology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

case and that most investigators are rapidly progressing to a common conclusion.

It has been definitely shown that the lower lumbar and lumbosacral articulations are responsible for symptoms in the majority of those cases suffering with the complaints already mentioned. Attributing such symptoms primarily to infection, muscle strain or mechanical disorders of the female pelvis is far less prevalent than it was a few years ago when a pain in the lower part of the back was too often taken as an indication for an investigation of practically all parts of the body except the spine.

Changes within the lumbosacral and less frequently other lumbar intervertebral disks are undoubtedly the cause of symptoms in more than 90 per cent of those patients who present themselves with any one or all of these complaints. Trauma is the etiologic factor in bringing about the changes within the disk in most cases. The various mechanical factors, which result in degenerative changes of the annulus fibrosus and in turn the nucleus pulposus, will be designated.

ACUTE TRAUMATIC DESTRUCTION OF THE INTERVERTEBRAL DISK

An acute traumatic rupture of the disk usually occurs between the ages of 10 and 25 years and is the result of a definite injury, the mechanics of which are compressive in character. In childhood and early adult life the nucleus pulposus of the lumbosacral disk is a definite fluid-like structure capable of resiliency and intervertebral support, therefore subject to rupture. Symptoms following the acute injury are often severe, but as a rule temporary in character. Later, varying from a few weeks to several years, usually while lifting a load, the patient again suffers an attack of pain in the lower part of the back. Such attacks may occur repeatedly and eventually are associated with an accompanying pain radiating down one and occasionally both extremities to the lateral aspect of the calf and ankle, following the fifth lumbar nerve distribution.

The most constant history associated with severe recurrent attacks of pain is that of some motion which involves hyperextension of the lumbosacral spine combined with a contraction of the erector spinae muscles.

Many acute ruptures would have been avoided had the compressive force been evenly distributed on the intervertebral disk, but in the presence of a static disturbance in the mechanics, the compressive force is applied primarily to one portion of the annulus fibrosus which ruptures under the strain. For this reason many disks which would eventually have given way to a chronic uneven distribution of weight are ruptured at an earlier period in life.

CHRONIC DESTRUCTION OF THE INTERVERTEBRAL DISK

Providing an individual, who presents a mechanical alteration and thus an uneven distribution of weight on the lumbosacral disk, does not suffer an acute injury, symptoms usually do not make their appearance until some time during the fourth decade of life. Such a patient may enter around the age of 35 giving a history of an acute sudden onset of pain following an injury. X-rays will show findings characteristic of a destruction of the disk, but associated changes give evidence that the process has been going on through the years, and for this reason the injury must be considered as only the factor which initiated clinical symptoms.

The commonest cause of an uneven distribution of weight on the intervertebral disk is a lordosis of the lumbosacral spine. Due to the erect posture of man which transmits the weight of the trunk to the posterior fibers of the annulus fibrosus of the lumbosacral disk, degenerative changes caused by stress have opened avenues of escape for the nuclear content and a fibrous degeneration has taken place by the time the individual has reached the age of 40. For this reason most individuals at this age period are potentially subject to pain in the lower part of the back. The stress on the posterior fibers of the lumbosacral disk is in proportion to the acuteness of the lumbosacral angle. Severe acuteness in the individual of the constitutional type who is short of stature, well nourished and presents firmly constructed joints and a good muscle tonus is due frequently to tight muscles and fascias in the anterior and lateral aspects of the thighs. The latter prevent an elevation of the front of the pelvis. In individuals of the constitutional type who are tall, thin and present long extremities and loose joints, the exaggerated lumbosacral angle appears to be due to a poor muscular tonus which causes them to assume a relaxed attitude in a position of balance while in the erect posture.

A lateral tilt of the first sacral vertebra due to a short leg or a developmental disturbance within the sacrum itself is the common cause

Fig. 1
Sacral obliquity resulting in chronic traumatic degeneration of the lumbosacral disk due to uneven distribution of weight. Note subluxation of lumbosacral facets.

of increased pressure on the lateral aspect of the lumbosacral disk. In maintaining the center of gravity over the base of support it is necessary to distribute the greater part of the weight of the trunk to that side of the intervertebral disk which corresponds to the high side of the sacrum. Barring an acute rupture of the disk as a result of a compressive injury in earlier life, these patients usually present first symptoms between the ages of 25 and 35 years. The x-rays show findings characteristic of a traumatic destruction of the lumbosacral intervertebral disk, details of which will later be discussed (*Fig. 1*).

The anomaly commonly spoken of as sacralization of the fifth lumbar vertebra is another cause of an uneven distribution of weight on the lower lumbar intervertebral disks. The fixation of this segment to the sacrum may be either unilateral or bilateral. When bilateral, the lumbosacral intervertebral disk retains a normal structure throughout life, but the articulation between the fourth and fifth vertebrae must compensate severely for the erect position, and in so doing the intervertebral disk at this site receives a severe stress on its posterior portion.

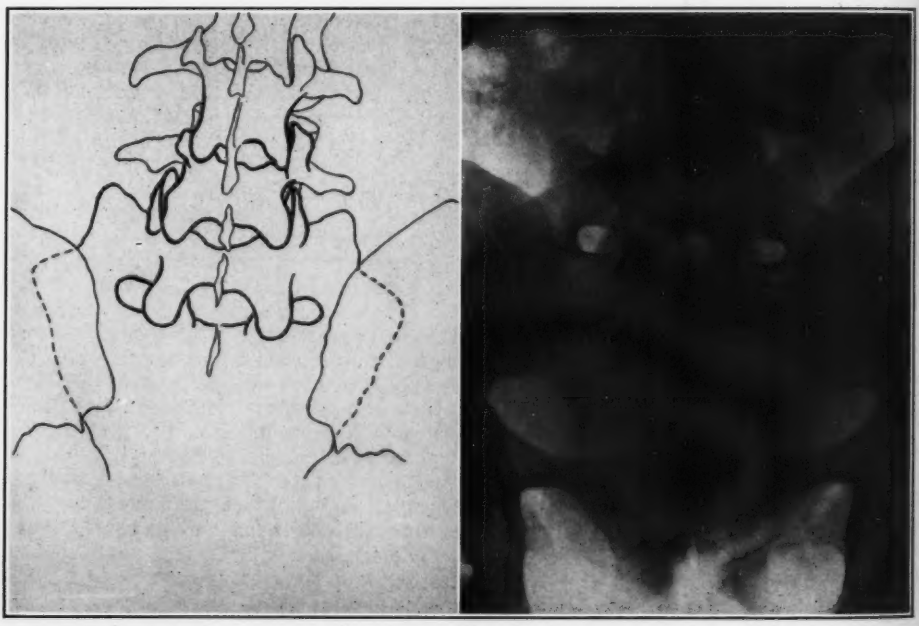

Fig. 2
Bilateral sacralization of the fifth lumbar segment, causing abnormal stress and resultant degeneration of fourth lumbar disk. Note subluxation of corresponding facets.

If not ruptured acutely in early life, chronic trauma brings about degenerative changes of the disk and clinical symptoms usually by the age of 30. Aside from localized symptoms, pain and frequently nerve changes follow primarily the distribution of the fourth lumbar nerve on either side and sometimes both (*Fig. 2*).

When the fifth lumbar vertebra is attached to the sacrum on one side only, in addition to the stress applied to the posterior portion of the fourth lumbar intervertebral disk, there is an abnormal stress taken on the free side of the lumbosacral intervertebral disk. Symptoms resulting from a settling of the free side of the fifth lumbar vertebra usually do not appear until after the age of 40. Segmental symptoms in such a case follow the distribution of the fifth lumbar nerve on the side opposite the fixation; however, for the reason already given this symptom may be combined with fourth lumbar nerve pain on either side (*Fig. 3*).

The anomaly spoken of as lumbarization of the first sacral segment is also capable of disturbing the weight-bearing mechanics at the lumbosacral articulation and thus causing an uneven distribution of weight on the intervertebral disk at this site. This condition may also be unilateral or bilateral. Whether unilateral or bilateral, the posterior fibers of the annulus fibrosus of the lumbosacral disk receive an abnormal stress from an uneven distribution of weight caused by an abnormally acute lumbosacral angle which these cases present. Unless ruptured early by an acute injury, degenerative changes have caused a settling of the disk, and clinical symptoms usually appear by the age of 35. Aside from localized pain, symptoms follow primarily the distribution of the fifth lumbar nerve on either side and sometimes both (*Fig. 4*). When the intervertebral disk between the first and second sacral segments is well developed and the segment is entirely free on one side, abnormal stress on the free side may cause a gradual settling, resulting in clinical symptoms following the distribution of the first sacral nerve on the free side. This particular symptom usually does not occur until after the age of 45, but earlier symptoms following the distribution of the fifth lumbar nerve may have been present at an earlier date for the reason already given (*Fig. 5*).

An infectious destruction of the lumbosacral

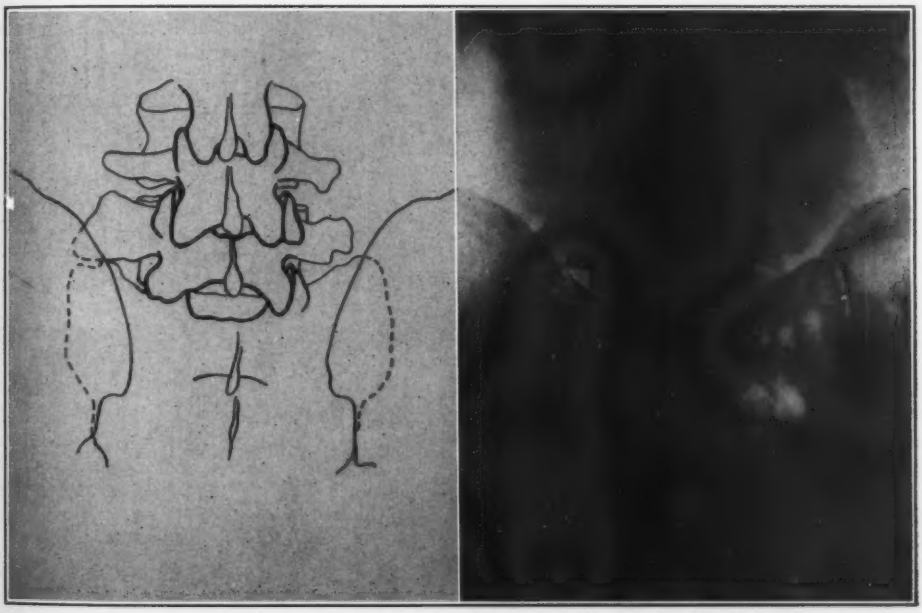

Fig. 3

Unilateral sacralization of the fifth lumbar segment, causing abnormal stress on the fourth lumbar disk and free side of fifth lumbar disk with resultant degeneration. Note subluxation of corresponding facets.

Fig. 4
Unilateral lumbarization of the first sacral segment, causing abnormal stress on the fifth lumbar disk and resultant degeneration. Note subluxation of corresponding facets.

intervertebral disk is occasionally seen and in early cases may be mistaken for the ordinary case which enters complaining of pain in the lower part of the back; however, the clinical course will usually differentiate it from the latter. The author has seen two cases of tuberculous destruction of the lumbosacral intervertebral disk which were treated for sciatica because of the segmental pain throughout the distribution of the fifth lumbar nerve, before the true nature of the lesion was recognized. Aside from tuberculosis the other commonest infectious destruction of the lumbosacral and other intervertebral disks is caused by the typhoid bacillus. The acuteness of pain and the inflammatory symptoms will readily differentiate the latter from the ordinary case.

Fig. 5
Unilateral lumbarization showing narrowed rudimentary intervertebral disk and subluxation of facets on free side (retouched).

Spondylolisthesis, while not a primary disk lesion, occurs to the extent of approximately 4 per cent and therefore should always be considered in those presenting themselves complaining of pain in the lower part of the back. In the author's experience segmental symptoms have not been a common finding in these cases. Pain in the lower part of the back radiating through to the abdomen, the anterior upper thigh and the groin is a more common complaint.

Fragmentation of the facets at the lumbosacral articulation constitutes less than 1 per cent of the patients entering with the complaint already outlined. When present, symptoms usu-

ally follow the distribution of the fifth lumbar nerve on the affected side.

X-Ray Changes.—It is the author's opinion that the recent inclination to insert an opaque oil into the neural canal in an effort to determine disk changes has been severely abused. A ruptured intervertebral disk at the lumbosacral or lower lumbar articulations can be interpreted by facet changes providing a proper x-ray technic is employed. Repeated careful clinical examinations will afford adequate information to determine whether the prolapse of the disk itself is sufficient to be of clinical significance. When the supportive structure of the nucleus pulposus is lost there is an immediate settling of the vertebra above, which is always registered on the corresponding facets when stress is being applied. Therefore either weight-bearing or in reclining, an extended position of the low spine is essential in obtaining proper facet relationship. All studies taken for the purpose of facet readings should be stereoscopic. Best results are obtained by a rotating anode tube. The patient should be posed in such a position that superimposed bony structures are minimal.

Narrowing of the intervertebral joint space is not so important in an interpretation of x-ray studies as are the facet articulations. This is due to the fact that a settling of the disk is frequently stopped by contact of bony structures. Therefore, primary attention should be focused on the articular facets in an effort to determine whether there is an overriding of these processes as shown in *Fig. 6*. Frequently the first sacral facets lodge in the inferior vertebral notches before an appreciable narrowing of the disk is apparent (*Fig. 7*). Under such conditions they become weight-bearing structures and produce a scarring of the vertebral notches of the fifth lumbar vertebra as well as a sclerosis of the superior margins of the first sacral facets themselves. In the anteroposterior study, this sclerotic change presents an irregular line at the junction of the lamina and the inferior articular facet of the fifth lumbar vertebra which may be misinterpreted as a fracture. In addition, the bony irritation in the inferior vertebral notch may result in a spur formation as shown in *Fig. 8*.

When settling of the segment above is stopped by lodging of the superior facets of the segment below the inferior facets of the above segments frequently appear atrophic when viewed by x-ray studies. This is due to the fact that the superior facets of the lower segment become weight-bearing structures and have taken over the load,

Fig. 6
Traumatic degeneration of the lumbosacral intervertebral disk as indicated by subluxation of the lumbosacral facets (retouched).

Fig. 7
First sacral facet lodged in inferior vertebral notches. This prevents further settling of the intervertebral disk.

thus removing the stress from the inferior facets of the above segment.

The degree of narrowing of the lumbosacral space depends primarily on the acuteness of the lumbosacral angle and the magnitude of the first sacral facets. When the lumbosacral angle is acute and the superior first sacral facets are large the latter will lodge in the inferior vertebral notches before the narrowing of the disk has become greatly apparent or in extreme cases even before the narrowing has become appreciable (*Figs. 9, 10, 11* and *12*).

Occasionally the spinous processes, when large,

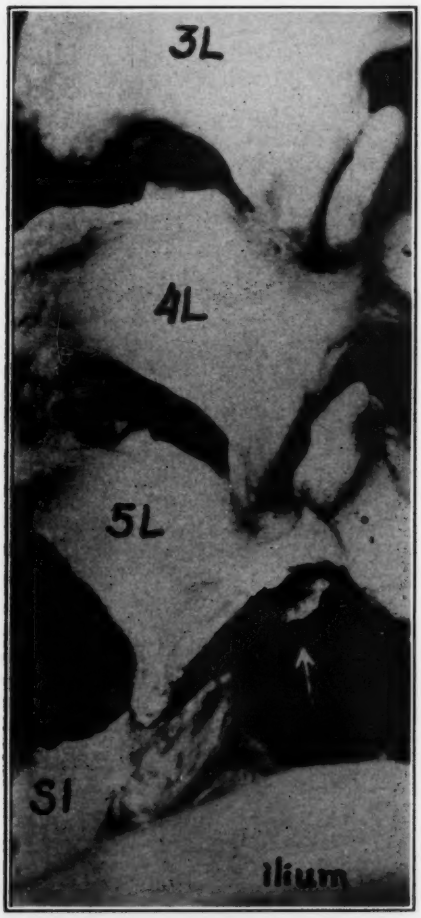

Fig. 8

Lodging of the superior first sacral facets causes sclerotic changes and spur formation in the inferior vertebral notch of the fifth lumbar segment.

Fig. 9

A complete loss of the joint space follows a destruction of the lumbosacral disk when the lumbosacral angle is not acute and the superior first sacral facets are not large.

Fig. 10

A complete loss of only the posterior portion of the joint space follows a destruction of the lumbosacral disk when the lumbosacral angle is acute and the first sacral facets are large.

contact each other and prevent further settling of the disk (*Fig. 13*).

Marginal lipping around the inferior and superior borders of the vertebral bodies adjoining the affected disk is the result of abnormal stress on bony structures which has resulted from a loss of the resilient intervertebral disk.

THE CAUSE OF SYMPTOMS

It is the opinion of many investigators today that disk changes account for symptoms in most of the cases frequently referred to as sciatica and lumbago. There is yet considerable confusion as to what change results in the segmental symptoms which these patients present. It is the author's opinion that they are due primarily to resultant disturbances in the mechanics in the lower part of the spine and that to ignore these and remove a prolapsed disk will result in persistent local and segmental symptoms following such surgical procedures.

The lumbosacral intervertebral disk undoubtedly suffers more from trauma than any other disk within the spine. The reasons for this are too apparent to be enumerated in this paper. A careful study of the anatomy of this region will reveal that the prolapse of the annulus fibrosus or the nucleus will not contact the fifth nerve root, yet none can deny that most cases present segmental symptoms throughout the distribution of this segment. The nerve emerges from the canal just below the inferior vertebral notch and contacts only the lateral aspect of the lumbosacral disk.

Fig. 11

From a lateral view the joint space appears to be preserved following a destruction of the disk when the lumbosacral angle is severely acute and the first sacral facets are large. Fig. 12 shows an AP view of this same case.

Fig. 12

Same case as shown in Fig. 11. Note marked subluxation of lumbosacral facets. The first sacral facets have lodged in the inferior vertebral notches of the fifth lumbar segment and prevented further narrowing of the joint space.

Fig. 13

Lateral view showing findings characteristic of a rupture of both the fourth and fifth lumbar disks. Further settling of the fifth lumbar segment is prevented by lodging of the first sacral facets. Further settling of the fourth lumbar segment is prevented by contact of the fourth and fifth lumbar spinous processes.

We should bear in mind that below the cord we are dealing with a bundle of nerve segments bathed in spinal fluid and confined in an area of the spinal canal which has been enlarged by nature to accommodate mobility at this site. Because of this, slight displacement from within would not be expected to cause symptoms so severe as at a higher level. If the magnitude of the protruding disk is great enough, an irritation of the meninges would be expected. This should cause a wider spread distribution of symptoms than most of the cases present when once they become chronic. It is probable that the extensive distribution of pain occasionally seen in those patients who have suffered their original injury is due to such an irritation; however, symptoms usually subside in these cases and the fixed segmental pain follows months or years later. The funicular portion of the nerve should be more subject to irritation than the intraspinal portion since it is not protected by spinal fluid. It is more logical to conclude that such symptoms are due to progressive changes which follow the rupture of the disk. When once the nucleus ruptures the annulus fibrosus undergoes an atrophic degeneration which results in a gradual narrowing of the intervertebral space providing stress is continued and not interfered with by the contact of certain bony structures. From anatomical studies, it becomes apparent that as the disk settles there results a subluxation of the lumbosacral facets and that the first sacral facets may directly contact the funicular portion of the nerve as it emerges through the lumbosacral foramen (*Fig. 14*). With such a mechanical situation hyperextensive motions of the low spine may result in an impingement of the nerve root. A careful study of the histories of these patients will reveal that recurrent attacks accompany a contraction of the erector spinae muscles at a time when the lumbosacral spine is in an extended position. Examples are lifting a load above the waist line, pivoting on a golf drive and raising a window.

Fig. 14
Anatomical specimen showing subluxation of the lumbosacral facets and impingement of the fifth lumbar nerve by the first sacral facet. (Courtesy of Dr. Yglesias.)

In two patients who presented severe fifth lumbar segmental symptoms, a fusion was accomplished without relief of symptoms. A second operation consisting only of a removal of the lumbosacral facets on the side affected afforded complete relief.

Over a period of eight years the facets have been removed and a graft placed in thirty-two patients. All, save one who died postoperatively, obtained relief of segmental symptoms.

It is the author's opinion that in better than 95 per cent of the cases, pain is due to mechanical alterations which have resulted in a constriction of the foramina and an impingement of the nerve root rather than to the prolapse of the disk itself. During the past year there have been two cases in which symptoms were such that they indicated pressure within the canal. Both were referred to a neural surgeon, who did a laminectomy. One revealed a nucleus pulposus which had become completely separated from the intervertebral disk and was lodged in the foramen around the nerve root. A fusion was done at the time and a relief of symptoms has resulted. The other presented a chondroma of the disk protruding posteriorly. It was removed and mechanics otherwise ignored. The patient, although considerably improved, continues to have segmental pain. Both cases presented a clinical picture which, when observed over a period of time, could not be confused with the usual case. Another patient under observation for the past year who was operated elsewhere eighteen months ago, the operation consisting only of a removal of the prolapsed disk, continues to present pain and nerve changes throughout the distribution of the fifth lumbar nerve.

TREATMENT

All cases should be given a prolonged conservative treatment before any radical measures are considered. With a thorough conservative program, better than 90 per cent of the cases will be relieved to the extent that they are happy to continue without surgery. This depends to a considerable extent on the occupation of the patient. Where heavy lifting is necessary it is difficult to control the mechanics of the lower spine. Conservative methods are based on reducing the lumbosacral angle and thereby lifting the weight from the posterior structures at this site. This means that the lordosis of the lower spine must be reduced to a minimum at all times, thus flexion of the hips is preferable when reclining. A slightly slumped position is desirable in sitting and in standing a straight lumbar spine is indicated. Lifting should be done without extending the low back and patients with such a lesion should always avoid bending backward. Spinal surgery should never be employed until a thorough conservative program has overcome a fixed lumbosacral lordosis and lengthened short fascias and muscles of the anterior and lateral aspect of the thigh. The latter may require severing as described by Ober.* If this is not done, pain just above the graft or at the lumbosacral joints due to a downward pull on the front of the pelvis may either persist or make its appearance following surgery of the lumbosacral spine.

One should have a thorough understanding of segmental symptoms before spinal surgery is attempted. Such surgery should consist of relieving nerve root irritation by removing the facets which correspond to the segmental distribution of pain and nerve changes and at the same time laying a lumbosacral graft. In those few cases presenting symptoms more suggestive of a spinal cord tumor due to fixed pain and nerve changes as well as spinal fluid changes, there is an indication for an opaque oil in the neural canal in order to gain a better understanding of the pathologic change before surgery is undertaken. When such surgery is indicated the mechanics of the low spine should not be overlooked. A graft should be placed and a facetectomy usually performed if we are to avoid postoperative symptoms.

*Ober, F. R.: Back Strain and Sciatica. J.A.M.A., **104**:1580, 1935.

DISCUSSION (*Abstract*)

Dr. Wendell G. Scott, St. Louis, Mo.—Dr. Williams notes that we have to study these patients not only from an anatomic aspect, but also from a physiologic and dynamic point of view. The problem of posture and habitus enters the picture. In the interpretation of the roentgenograms we must keep in mind how the mechanics of posture may influence the anatomic diagnosis.

As regards intraspinal protrusions of the intervertebral disk, I think it was well emphasized that only a small percentage of all patients who have back pain will exhibit a protrusion of the disk into the spinal canal. In our clinic the selections of patients for spinal myelography is determined largely by one fact, namely: if the patient has been examined by a competent orthopedist and has been thoroughly treated without relief, such a patient becomes a candidate for myelography. I was also glad to hear Dr. Williams say that you cannot diagnose the presence of a protruded disk simply because the disk is narrowed. We have all examined cases with a narrowed disk without detecting a posterior protrusion of the disk.

In doing spinal myelography, we like to make films with the patient in the lateral position, first with the spine flexed and then with the spine extended to determine if a protruded disk is reducible. If it is reducible, maybe the orthopedist can treat the patient and prevent an operation. If it is not reducible, then that is a very definite indication for operation. I believe, too, that a protruded disk can produce definite pressure on the nerve root. At operation the nerve root is often pressed up against the margins of the spinal canal by a portion of the disk. I believe this pressure is the cause of pain.

I was very much interested in Dr. Williams' ideas concerning the apophyseal joints as a cause of pain, and particularly their subluxation. One must be extremely careful of making a diagnosis of apophyseal subluxation. By taking radiographs of a patient's spine when tilted to one side, and also in flexion and extension of the spine, one will see a wide range in the mobility of normal apophyseal joints.

I am wondering how frequently the neurosurgeon or the orthopedist finds a definite compression of a lumbar nerve root as it passes through the intervertebral arch. I have not heard of many such reports from the group we are associated with. From the pathologic specimen Dr. Williams showed, they do occur.

Dr. Williams (closing).—Overriding of the lumbosacral facets is frequently observed in x-rays of patients who, at the time, do not present clinical symptoms. However, I consider all such lesions potentially painful and a detailed history will usually reveal intermittent attacks of pain following a strain of the lumbosacral spine. It is the duty of the clinician to determine the presence or absence of symptoms at the time of the examination. The radiologist can do no more than call attention to the fact that the lesion is present and even in so doing he occasionally is likely to become involved in controversies when dealing with industrial cases.

FRACTURES OF THE NECK OF THE FEMUR*

By JARRELL PENN, M.D.
Knoxville, Tennessee

It is somewhat apologetically that I present another paper on the subject of fractures of the neck of the femur to the Bone and Joint Section of the Southern Medical Association. However, since the Fracture Committee of the American Academy of Orthopedic Surgeons reported that of two hundred surgeons responding to questionnaires concerning internal fixation of these fractures, one hundred stated that they had not used this method of fixation, two of whom volunteered the information that they hoped they never would, and since I have had two interesting experiences in my small series of cases that might be worth calling to your attention, I feel perhaps I am justified in reopening this much-discussed question.

In his classical address before the Clinical Congress of the American College of Surgeons in Boston in 1934, Kellogg Speed named this "The Unsolved Fracture." Unsolved because after more than a quarter of a century of almost universal adoption of the Whitman abduction plaster method of managing these injuries between 40 and 50 per cent of them have resulted in failure. It is true that isolated series reported by certain clinics have enjoyed a much higher percentage of success. A few have reported that they have had no nonunions, but this is certainly the exception rather than the rule.

All of these failures cannot be charged to mismanagement, because many surgeons or groups of surgeons who obtain satisfactory results in other fractures are disappointed with the outcome of their femoral neck fractures despite the same diligence and the same meticulous attention to detail here as elsewhere. There must be some intrinsic peculiarity of the head and neck of the femur that renders these fractures less amenable to the customary methods of treatment.

I believe it is generally agreed that the most important of these intrinsic peculiarities is the anatomical arrangement of the circulation to the capital fragment. Albee stressed the importance of the patent vessel in the ligamentum teres. He feels that severance of this vessel is largely, if not wholly, responsible for the aseptic necrosis of the femoral head which is frequently seen. Most observers who have availed themselves of the opportunity to study the circulation of the head and neck of the femur do not deny the presence of this vessel and its aid in nourishing the femoral head. However, it is their opinion that the major nutrition is derived from the nutrient and capsular vessels entering the neck distal to the head flowing backward into the femoral head. This blood supply is interrupted on fracture with separation of the fragments, the ischemia being more complete the nearer the fracture is to the head. For the most part, the capital fragment must be revitalized by a new blood supply crossing the fracture line growing into and revascularizing the head.

Doubtless many of these failures followed incomplete reduction, an error quite easily and innocently made before lateral, as well as anteroposterior, x-ray views became routine. One must be an extreme optimist to expect the newly formed vessels to bridge a gap to revascularize the displaced head. If the Whitman cast were still our method of choice, our results would surely be improved if accurate anatomical approximation were demonstrated in both the anteroposterior and lateral x-ray projections.

On opening fresh fractures of the neck of the femur, capsular tags have been found interposed between the fragments in many cases. The interposition of soft tissue is certainly not conducive to success in healing of any fracture, especially these most difficult ones.

Gaenslen has demonstrated that reduction of femoral neck fractures by traction with the hip and knee flexed at right angles withdraws most of these capsular tags from between the fragments. He believes that this position is so important that he inserts his internal fixation material while the limb is maintained in the position of right angle flexion of the hip and knee. If, however, accurate anatomical reduction is obtained with the hip and knee flexed at right angles according to the method described by Leadbetter and this anatomical reduction maintained while the hip is being brought into the extended position, it is improbable that further soft tissue will be interposed between the fragments. It has been the experience of most operators that the hip can be safely extended before the operative procedure is undertaken.

Still another cause of our frequent failures is

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

the fact that it is impossible completely to immobilize these injuries in plaster even by the most careful application of a snug unpadded cast, because of both voluntary and involuntary contraction of the muscles surrounding the fracture, a fact that was brought home to me most forcefully by one of the cases reported below.

In addition to these local peculiarities, the prolonged period of immobilization in large plaster casts necessary in those elderly patients whose general metabolism is already at its lowest ebb frequently resulted in irreparable damage, although it cannot be denied that the Whitman cast was truly life-saving in innumerable instances before we had better means at our command.

With the perfection of internal fixation methods, many of these difficulties have been obviated. Certainly internal fixation cannot and does not restore the damaged blood supply to the head. It can and does adequately immobilize the fragments, however, so that the newly formed vascular buds are not sheared off as rapidly as they are formed. More accurate reduction has accompanied this method of treatment because almost all fixation materials are inserted under both anteroposterior and lateral x-ray control, instantly informing the surgeon if incomplete reduction is present. Soft tissue interposition is not likely if capsular tags are withdrawn from between the fragments by Leadbetter's manipulation before fixation. The contrast in the convalescence of these patients with early freedom of unrestricted motion in bed and in the wheel chair is striking when compared to the rigid confinement of the cast.

Internal fixation has not been in use long enough to make comparative end result studies with older methods. However, its use has already proven that the percentage of failures has been greatly reduced. A true comparative end result study can probably never be made, as I have not seen reported any large series of cases treated by the Whitman method having the advantage of lateral x-ray control.

It was not my original purpose to discuss methods or technic. I simply sought the opportunity to make a plea for the more universal adoption of internal fixation as the method of caring for these patients. However, after a rather careful review of the literature, the innumerable gadgets, devices and methods described have persuaded me also to make a plea for simplicity. All of these devices doubtless have merit, but to me many of them would merely tend to complicate a procedure that can be carried out with relative ease.

I have employed the uncannulated Smith-Petersen three-flanged nail in the majority of my cases, inserted according to the method described by Wescott with only slight modification. A marker is always placed over the anatomical location of the head of the femur and its position verified by the original postreduction x-ray film. The point of the nail is directed toward the marker, making corrections if necessary for its relation to the head. If, after the nail has been introduced into the bone, its direction is not satisfactory, little difficulty is encountered in its extraction for directional correction. I can see no objection to the use of a wire guide if one finds that it facilitates the introduction of the nail. However, I have never used them. Equally satisfactory results have been reported following the use of Moore's three nails and they are apparently introduced with the same simplicity in the hands of those trained in their use. I do not believe either of these procedures is attended with any more shock than the simple reduction of the fracture and the application of a Whitman spiker cast, and their use has proven far more satisfactory.

I have had no experience with the subcutaneous introduction of Kirschner wires or Steinmann pins in fixing these fractures. Key and others reporting a method employed in the St. Louis City Hospital in which two Steinmann pins were introduced subcutaneously into the femoral neck across the fracture line secured firm bony union in 45 per cent of a series of 29 cases. There were six deaths and if these are omitted, bony union took place in 58 per cent of their series. This is the highest percentage of failures I found reported in any series. Most of these patients were operated upon by the resident staff of the hospital and their failures have been attributed to: (1) poor general condition of the patient, (2) poor reduction, (3) faulty insertion of the pins, (4) failure of the pins to remain in position, and (5) bending of the pins. In addition to these, their failure also suggests to me that only two points of contact may be inadequate, and should this method be employed it would seem that three pins should be used to avoid the shearing motion between the fragments so revascularization of the head would not be disturbed. Other observers have reported the migration of these free pins into the pelvic

cavity and some means to prevent this complication should be employed with their use.

In closing, the following two cases will be reported:

Case 1.—G. T., a white man, 24 years of age, was admitted to the Knoxville General Hospital on July 4, 1938, with a history of having received an injury to his right hip in an automobile accident shortly before admission. On examination, it was found that the patient was a spastic paralytic with athetoid contraction of the muscles. The characteristic, physical and x-ray findings of a central fracture of the neck of the femur with separation of the fragments were present.

Fig. 1, Case 1
Central fracture, neck of femur, anteroposterior x-ray view before reduction.

He was taken to the operating room, where a Smith-Petersen nail was inserted with no difficulty and postoperative x-ray examination showed the fracture to be satisfactorily reduced and the nail in a good position. He was put to bed with no external support. On examination 48 hours later, the leg was found to be externally rotated, shortened and the patient complained of severe pain on the slightest motion of the injured extremity. A Thomas splint was applied and additional x-ray study made. To my surprise, I found the nail had been completely extruded from the capital fragment and, of course, was no longer immobilizing the fracture. He was again taken to the operating room, where the Smith-Petersen nail was removed and Moore's three nails inserted on the assumption that muscle contraction would have more difficulty in backing out the nails in three different planes. Following this procedure, a double spiker cast was also applied, hoping further to immobilize the fracture.

On the third day following the second operation further x-ray study was made, and it was found that two of these nails had been extruded from the capital fragment and the third had been sheared off at the site of fracture. The wound was reopened for the third time. The two whole nails and the trochanteric half of the third nail were removed. No further effort at internal fixation was attempted. The wound was closed and the hip immobilized in a plaster of Paris cast.

Unfortunately, infection followed the third operative interference which went on to osteomyelitis of the trochanter, septicemia and death on November 29, 1938. However, the patient demonstrated to me the fact that muscle action is a real problem in attempting adequately to immobilize these fractures.

Should I be faced with the same problem again, I believe I would insert the Smith-Petersen nail and immediately apply traction to the injured extremity in an effort to fatigue these powerful muscles despite the fact that this is the one fracture in which traction is contraindicated except in children. I have not used external support in these cases other than sand bags for

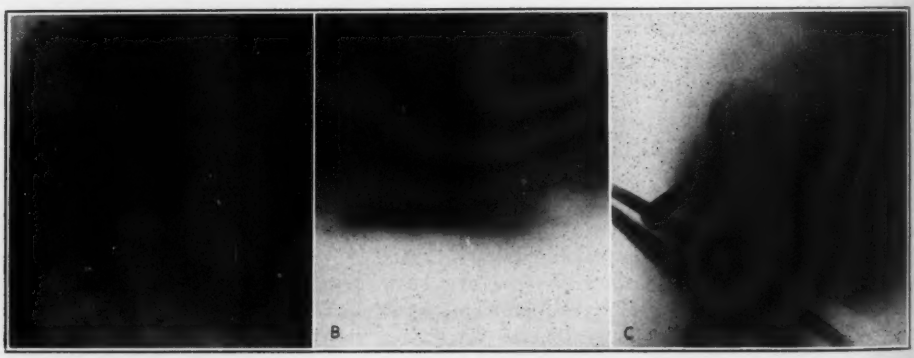

Fig. 2, Case 1
(A) Anteroposterior view after reduction and insertion of Smith-Petersen nail; (B) lateral view following reduction and insertion of Smith-Petersen nail; (C) anteroposterior view forty-eight hours after operation showing nail extruded by muscle pull.

the first day or two. However, after this experience, I doubt the wisdom of not immobilizing them at least for a few days.

Case 2.—K. W., 70 years of age, was admitted to Fort Sanders Hospital, November 11, 1936, with a typical fracture of the neck of the femur with separation of the fragments. She is the last patient I have treated by Whitman's method, but after three or four months union appeared to be satisfactory and the cast was removed. She received the usual postoperative care and was allowed to begin weight-bearing at the end of the sixth or seventh month. On June 16, 1937, only eight months following the original injury, I was notified that she had broken her hip again and had been readmitted to the hospital. On x ray examination following the second injury, however, it was found that the old fracture of the neck of the femur had not been injured, but that she had received an intertrochanteric fracture of the same femur. This injury was also treated in a plaster spiker, resulting in a firm bony union, allowing the patient to be up and about on the injured extremity until she died some two or three years later of pneumonia.

I was glad of the opportunity to observe the fact that if union does take place, the femoral neck obtains its original strength and resistance to subsequent injury.

CONCLUSION

The ultimate solution of the problem of fractures of the neck of the femur may not as yet

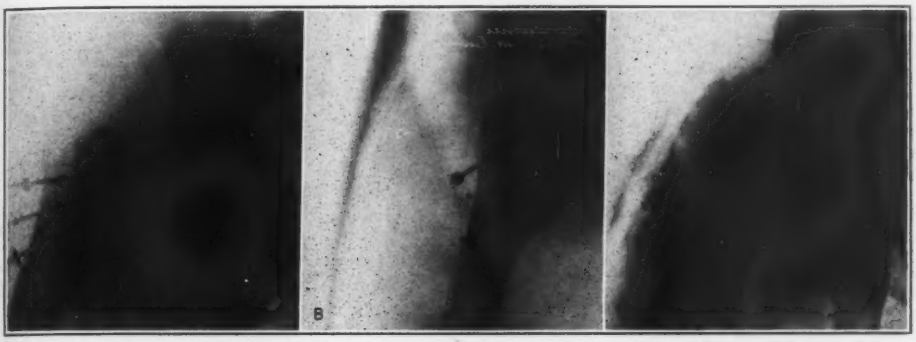

Fig. 3, Case 1

(A) Anteroposterior view following second operation after insertion of Moore's three nails; (B) anteroposterior view seventy-two hours after second operation showing two of nails extruded and the third sheared off at the site of fracture; (C) anteroposterior view following the removal of the two extruded nails and the trochanteric half of the broken nail.

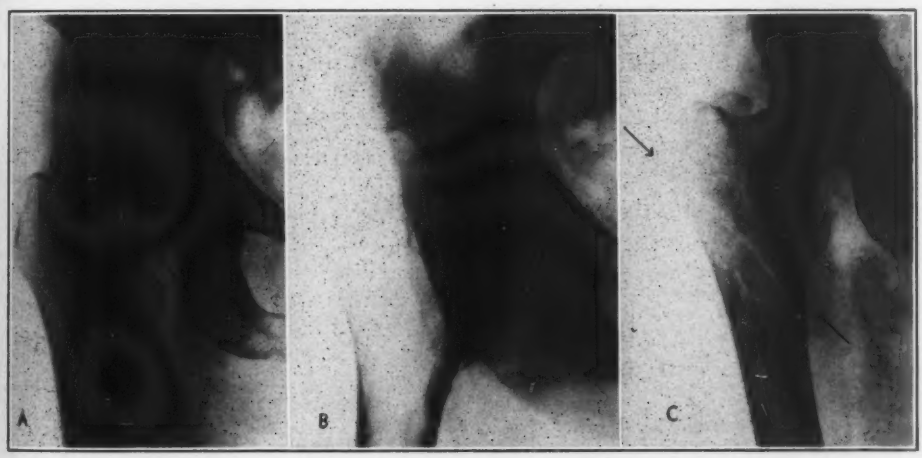

Fig. 4, Case 2

(A) Anteroposterior view of central fracture through neck of femur before reduction; (B) anteroposterior view four months following original injury; (C) anteroposterior view immediately following second injury, eight months after original injury showing the original central fracture of the neck of the femur was not disturbed, but an intertrochanteric fracture occurred.

have been found, but adequate internal fixation obviates many of the difficulties previously encountered and apparently is greatly increasing the percentage of good results in these cases.

DISCUSSION (*Abstract*)

Dr. Henry G. Hill, Memphis, Tenn.—The treatment of fresh fractures of the neck of the femur has long been a major problem in orthopedic surgery. One of the principal reasons for this is the fact that the large majority of individuals who sustain such a fracture are advanced in years and often afflicted with systemic diseases in addition to the usual physical and metabolic changes of senility. Nor is this feature of the problem likely to be soon altered. On the contrary, since statistics indicate that the average span of life is constantly increasing, we may expect a correspondingly increasing number of fractures of this type in the aged. Any measure which will ameliorate or circumvent the adverse influence of these pre-existent handicaps to the successful treatment of such fractures should receive our active endorsement. Such a measure seems to have been found in modern methods of internal fixation.

The introduction of the Smith-Petersen nail, in 1931, as a means of internal fixation of fractures of the neck of the femur may be said to have inaugurated a new era in the treatment of this injury. Prior to that time, internal fixation had been practiced to a limited extent in this country and in Europe. The procedure was a formidable one, however, and the results did not justify its general adoption. Indeed, as first employed by Smith-Petersen, the operation was too extensive to be undertaken except in favorable cases, as the nail was inserted through an intracapsular approach to the femur. This technic is still followed by a few surgeons, but has been abandoned by the majority, including Smith-Petersen himself, in favor of the less traumatizing extracapsular approach, as devised by Johannson.

Within the past few years a variety of methods of internal fixation have been advanced, all based upon Smith-Petersen's original principal. Kirschner wires, nails, pins, spikes and screws of different types have been employed and, with the exception of Kirschner wires, generally with gratifying success. Most authors have found the wires unsatisfactory in that they lack rigidity and have a tendency to wander.

In the opinion of some authors, proper reduction of the fracture and accurate insertion of the nail will be followed by union in every case. This seems an over-optimistic view. We have recently observed a man 32 years of age with nonunion and persistent pain six months after an excellent reduction and fixation with a vitallium nail. Although accurate reduction and fixation are of primary importance, obviously, other factors, such as careful postoperative attention and prevention of too early weight-bearing, are vitally involved in the outcome. The success of internal fixation probably should not be gauged solely by the extent of bony union, but rather by the degree of function, since in older people solid union may not take place, leaving the nail to be chiefly instrumental in maintaining a useful extremity. This would appear to be a logical view; not infrequently a strong fibrous union is sufficient for the normal activity of an elderly individual.

From the surgical standpoint, the operation of extracapsular internal fixation meets every requirement. Royal Whitman, in speaking of the campaign for the establishment of surgical principles in the treatment of this fracture, makes the following statement: "The fact that what was formerly the most neglected of all fractures can now command the technical skill required for the spiking operation is conclusive evidence that the campaign which has been carried on for upwards of a half century has been successfully concluded." We agree with Whitman and others that it is yet too early to judge conclusively the outcome of internal fixation, but if, all things being equal, we can safely promise restoration of a useful member in an appreciably larger number of cases than by treatment with other methods, in addition to a comfortable convalescence and one of comparatively short duration, with minimum danger of infection and impairment of muscle tone and joint motion, and, finally, a negligible risk of life, we may rightly feel that the procedure offers a solution of the problem of fractures of the neck of the femur.

Dr. F. Walter Carruthers, Little Rock, Ark.—One point that has always been uppermost in my mind and which has been brought most forcefully to my attention in handling certain fractures of the neck of the femur in aged individuals is whether or not we should be more particular as to the type of pin or nail to be used in certain cases.

I have had the misfortune on one or two occasions in nailing an elderly individual with a Smith-Petersen nail to have the greater trochanter split out, due, of course, to the brittleness of the bone and the thinness of the cortex.

Since that time I have tried to be more meticulous in my selection, especially in old persons whose cortex I know to be thin, and instead of the Smith-Petersen nail I have found it more successful to use either the Moore nails or the Knowles pins. I have had no misfortune with the use of either of these types.

Three weeks ago I nailed a "young boy," aged 91 years, using three Moore nails. X-rays made before and after nailing by this method show, in addition to the fracture, the calcification and deposit in the femoral arteries, which emphasize his age.

It has been three weeks since the hip was nailed and he is able to sit up in a wheel chair daily.

If the nail in the hip of an elderly person bursts out, it certainly is a pitiful state.

I believe, therefore, that we should show a little more care and judgment in selecting the type of nail we are to use.

Dr. Harold B. Boyd, Memphis, Tenn.—About three months ago I had the privilege of studying the cases that have been treated by the staff of the Willis C. Campbell Clinic. At that time, 115 fractures of the neck of the femur had been treated in which the Smith-Petersen nail was used. This series embraced only true fractures of the neck of the femur with displacement; impacted fractures, those at the base of the neck, and trochanteric fractures were excluded. According to Pauwel's classification, they were all type 2 or 3. It is interesting to note that the type 3 fractures constituted 12 per cent of the series. The oblique fracture with the resulting pear shaped proximal fragment seen in this type produces the maximum amount of shearing force encountered in a fracture of the neck of the femur. Both from a theoretical and practical standpoint, the prognosis is poorer in this group.

The mortality for the series was 5.7 per cent in the first postoperative month; only 10.2 per cent for the first six months postoperative. The hospital mortality is approximately one half that incident to treatment by the Whitman and other so-called conservative methods.

Fifty-five of these patients returned sufficiently long after the insertion of the nail to determine whether or not they would secure bony union. Of these, 86.5 per cent had bony union and 13.5 per cent had nonunion or fibrous union.

Of the cases that had bony union, 15.5 per cent had traumatic arthritis. All the cases that showed these changes, except one, had secured union in the presence of aseptic necrosis of the head of the femur. If future experience reveals that the majority of arthritic changes are secondary to unions in cases with aseptic necrosis of the head of the femur, it may be possible to minimize the arthritic changes by postponing weight bearing over a sufficient period of time to permit revascularization of the head of the femur.

The percentage of arthritic changes will in all probability increase as statistics over longer postoperative periods are compiled, as these changes are produced by long continued weight bearing. As suggested above, the percentage of arthritic changes in those cases with aseptic necrosis of the head of the femur may be minimized by increasing the length of time before weight bearing is permitted.

Dr. C. J. Frankel, St. Louis, Mo.—I was a member of the house staff of the city hospital that Dr. Penn referred to at the time those figures were compiled. We always underestimated rather than overestimated our results.

I had the opportunity of posting one of those cases in which one of the pins had pierced one of the iliac veins. The man, I believe, died about 24 hours after the pin had been placed in there.

Since the method has been changed, results in the hospital are comparable with other hospitals of the country.

Dr. Gordon King, Jacksonville, Fla.—As I understand it, the muscle pull gives considerable worry in this type of case. I should like to ask whether any work has been done using temporary block of the muscles to discontinue this pull for a long enough period to help out with union.

Dr. Austin T. Moore, Columbia, S. C.—I am becoming more and more convinced that the problem in these hip cases is purely and simply a mechanical one, which is dependent on a good reduction and perfect immobilization over a sufficient period of time. I believe that if this is carried out, there will be solid union in almost 100 per cent of the cases. I do not feel that the blood supply to the neck is the important factor because one may have union in a fracture of the neck of the femur with an avascular head if it is perfectly reduced and rigidly immobilized.

I have been using four nails placed parallel, two above and two below, making a parallelogram with the nails, all four of which are fixed firmly into the hard portion of the head. These four nails will take all stresses and strains and their position is like the placement of steel in concrete pillars. From a mechanical standpoint, the more widely apart the four nails are placed the greater the strain which they will take and the more rigid the fixation will be. The upper two nails will take the tension stress, and the lower two nails will take the compression stress. The four nails will together take the rotary and sheering stress. The neutral axis of the bone is directly in the center of the neck and any internal fixation exactly along this imaginary line will take no stress or strain and is theoretically useless. We have observed in some of our earlier cases with three nails bunched together in the center of the neck and head, that there is very poor fixation and there subsequently will be absorption of the neck.

After reviewing our cases, we feel that we can look immediately at the fixation as soon as it is done and anticipate whether or not there will be a good result.

I want to mention intertrochanteric fractures. We use multiple nails and frequently make a little bolt by using two nuts on one nail. I think the intertrochanteric fracture is the most satisfactory of all to treat.

Dr. Penn (closing).—So far as I know, muscle block has never been done and I do not believe such a procedure would be necessary. I have never had trouble with muscle action's disturbing the position of the Smith-Petersen nail except in the spastic case reported today. This case demonstrates the powerful action of the strong hip muscles but some form of simple external support should be sufficient to control them.

PRIMARY JEJUNAL ULCER*

By F. Eugene Zemp, M.D., F.A.C.P.
Columbia, South Carolina

Probably no part of the gastro-intestinal tract receives less attention, less thought, and less study than the jejunum. When we realize the vast function of this organ we see that it is fortunate indeed that it is not more often the seat of disease. Such lesions as congenital anomalies, enteritis, obstruction from adhesions, primary carcinoma, sarcoma, benign tumors, polyps, diverticula, ulceration in systemic diseases, ulcers following gastrojejunostomy occur, but primary jejunal ulcer is extremely rare. Its clinical signs are fairly characteristic and differ considerably from ulcers involving other parts of the alimentary tract. Rufz[1] is generally credited with calling our attention to ulcers in the jejunum when he reported a case in 1843. Richardson[2] collected 12 cases in 1922, and in 1924 Brown[3] reported 35 cases of simple ulceration of the jejunum and ileum, 9 of which occurred in the jejunum. In 1933, Ebeling[4] made a thorough study of the subject, surveying both domestic and foreign literature and presented a summary of the important findings in 47 cases, including

*Read in Section on Gastroenterology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

one of his own. He omitted a case reported by Heinatz[5] in 1928. Since then Coletti[6] has reported two cases and Puhl,[7] Hall,[8] Desjacques,[9] Lastra,[10] Smith,[11] Harris[12] and I[13] have each reported a case in which there was a simple ulcer in the jejunum without ulceration in the remainder of the intestinal tract, and without any systemic disease or previous gastrojejunostomy. The detailed reports in recent years enable one to outline certain findings that are present in the majority of cases, which aid considerably in the diagnosis.

The importance of this type of ulcer is readily appreciated when one reviews its mortality. Of the fifty-two cases with sufficient data to be studied, twenty-eight died, making a total mortality of 53.8 per cent. There were forty-three perforated cases, of which twenty-three died, a mortality of 55.8 per cent. Twenty-five of the perforated group were operated upon with nine deaths, or a mortality of 36 per cent. Those operated upon within twenty-four hours had a much lower mortality. There were nine nonperforated cases, of which only one was correctly diagnosed before operation. All were operated upon with only one death, a mortality of 11.1 per cent. The above mortality is considerably less than that ten years ago.

Pathology.—The upper one-third of the jejunum was by far the commonest site. Sixty-eight per cent were situated in its proximal portion. The majority (83 per cent) were opposite the mesenteric attachment, and varied in size from 2 mm. to 2 cm. and usually were single. Eighty-six per cent were circular in shape with a clean-cut punched-out appearance, and on cross section were often terraced. This latter feature accounted for the minute perforations at times. There was usually some narrowing of the lumen due to the marked fibrosis that had developed over a considerable time. The majority perforated, sometimes very early, but as a rule not until after well developed fibrosis had taken place. Hemorrhage was rare, and none became cancerous. The regional lymph nodes were often enlarged and showed inflammatory changes. Microscopic studies showed a necrosis varying in depth from the mucosa to the serosa with round cell infiltration and fibrosis of varying degrees. Very few showed any change in the vascular system except an occasional thrombosis. The ulcer had not the appearance of those sometimes found in the jejunum in tertiary lues and Levaditi's technic was negative when done. The giant cells of tuberculosis were not seen.

Etiology.—I think one can state with certainty that the true cause is not known. All of the theories that have been advanced for the development of ulcers in other parts of the gastro-intestinal tract have been suggested, as emboli, vascular changes, endocrine disorders, streptococci, irritative action of the intestinal chyme, and so on. It is certainly possible that the initial factor may be the result of some previous disease of the intestinal tract, as the enteric fevers, amebic or bacillary dysentery and cholera. Heterotopic gastric mucosa was present in one (Puhl's[7] case). A focus of infection from which bacterial emboli are carried to the jejunum is possible. Smith's[11] case had thromboangiitis obliterans, but this condition was not evident in the ulcer, and in most of the cases there were no vascular changes. Trophic disturbances, trauma, and foreign bodies as a fish bone are mentioned. Abnormal acidity of the jejunal contents from pyloric dysfunction is inferred. Tuberculosis is possible and should be ruled out by detailed studies. Syphilis is difficult to exclude. The presence of a positive Wassermann does not mean that the ulcer is luetic. Spirochaetes should be found in the ulcer by Levaditi's method. The majority occurred between the ages of 31 and 60, with from 40 to 60 predominating. They were three times more frequent in males than in females.

Symptoms.—In seven cases there were no symptoms previous to a sudden rupture, but the remaining patients had had indigestion and abdominal distress from a few weeks to a year or more. Pain was usually present in the mid-epigastrium or was periumbilical. Sometimes it was general abdominal, in the left upper or lower quadrant, and occasionally in the right or in the back. It was characteristically described as hurting, colicky, cramp-like, or boring. In about 12 per cent the pain resembled that of duodenal ulcer, occurring 2½ to 3 hours after meals when the ulcer was very near the duodenum. Food sometimes relieved it and sometimes aggravated it. Gas, heart burn, sour stomach, belching, nausea, vomiting and constipation were frequent. Two cases had bleeding and one had hiccoughs. As the ulcer progressed with the development of stenosis, subacute high obstructive symptoms appeared; colicky pains, belching, nausea, vomiting, distention (upper abdominal), constipation, rather marked, and visi-

ble peristalsis. Movement of the bowels, particularly after a laxative, usually aggravated the pain and the peristalsis. Acute perforation occurred in all but nine cases and was ushered in with a sudden and severe pain in the mid-abdomen, soon becoming generalized. In several cases the pain radiated to the left side, and in only one case did it localize in the right lower quadrant. There was also shock, board-like rigidity, tenderness and usually a diminution of liver dullness. Those in whom operation was delayed or who were not operated upon at all developed the usual signs of a general peritonitis.

Diagnosis.—A careful history of chronicity of symptoms should make one suspicious. The subacute obstructive signs of upper jejunal involvement should be easily recognized, as well as the signs of acute perforation. The laboratory studies aid very little, for the gastric analysis is usually low and there is no change in the blood count, except in perforated cases. Fluoroscopic examination frequently gives the diagnosis in the non-perforated cases. Studies of the jejunum 5 hours after the opaque meal often show a regurgitation with stasis and dilatation proximal to the lesion. Occasionally the ulcer may be demonstrated, but more often narrowing of the lumen is present due to the stenosis. If the obstruction is complete, a plain roentgenogram will often show the jejunal pattern containing air. In the perforated cases a roentgenogram in the erect position will show an air bubble under the dome of the diaphragm. At operation a thick ropy mucoid exudate is usually found.

Treatment.—Medical treatment is of no value in the majority of cases. As soon as the diagnosis is made of either the perforated or non-perforated cases, operation should be performed. In the non-perforated cases, a resection of the ulcer-bearing area is preferred. In the perforated cases oversewing and drainage are usually done. Sometimes a resection with lateral anastomosis is necessary.

CASE REPORT[13]

E. B. R., a white man, 59 years of age, complained of pain in the lower abdomen. The family history was negative. In the past history he had the usual childhood diseases and typhoid fever at the age of 10. Twenty years before he had a severe case of diarrhea, which lasted three weeks and was undiagnosed. There had been no operations or injuries. He drank four or five cups of coffee a day, occasionally tea, coca-colas and cocktails, and smoked rather heavily, about thirty cigarettes a day. He slept well, but was of a nervous temperament, easily upset and had lost fourteen pounds during the past year. The present illness began nine years earlier with pain in the lower abdomen, which was spasmodic in character and occurred at varying intervals. During the previous five months the pains were very severe and caused him considerable discomfort. They were described as colicky and occasionally there was a gnawing or burning sensation in the epigastric region, not related to eating. Lying on his stomach gave some relief, and complete relief from a few days to a week or more occurred at various intervals. His appetite was good and there was no nausea or vomiting, but considerable gas with distention. Although constipated most of the time, he occasionally had a watery stool. Immediately after a bowel movement his abdomen often became distended, especially if a laxative had been taken.

On physical examination he was 6 feet 1½ inches, weighed 142 pounds, and was somewhat pale. His scalp, ears and nose were negative. The pupils were normal in size and shape and reacted promptly to light. There was no exophthalmus or icterus. The eyegrounds were negative. His teeth were false and throat negative. There were no enlarged lymph nodes in the neck, but in the isthmus of the thyroid gland was a small hard nodule about the size of a marble. The chest was well nourished and developed. Expansion was good and the lungs were clear. There was no enlargement of the heart and its action was normal. The blood pressure was 132/70. The abdomen was slightly scaphoid in shape, soft and relaxed, and no masses were palpable. The abdominal aorta was palpable and descending colon contracted. The liver edge could not be felt and there was no tenderness over the gallbladder area. The spleen was not palpable and the kidneys were negative. The extremities were normal in size and shape and all reflexes were active and normal. The brachial arteries felt somewhat thickened and there was no epitrochlear glandular enlargement. The genitalia was normal, except for a slightly enlarged epididymis. The prostate gland was firm and the left lobe was slightly larger than the right. Proctoscopic examination revealed a normal mucous membrane.

In the laboratory studies the red blood cells were 3,890,000, hemoglobin 78 per cent, white blood cells 7,400 with 69 per cent polynuclears. The Wassermann and Kahn tests were negative. The urine had a specific gravity of 1.012, dark amber, acid, and did not contain any albumin or sugar. The microscopic study was normal. In the fractional gastric analysis the free hydrochloric acid ranged from 40 to 70 degrees, and the total acids from 60 to 78 degrees. On May 1, 1937, the examination was completed with a fluoroscopic study of the chest, stomach and duodenum. The findings were normal, except for a moderate ptosis. An x-ray of the genito-urinary tract was also normal.

My impression, after the examination, was of a moderate ptosis with hyperacidity and probably an ulcer, very small or not demonstrable. He was, therefore, placed on an ulcer diet with the usual alkalies. Slight improvement followed for two weeks, at which time visible peristaltic waves were noted in the mid-abdomen. Because of this, a barium enema was given, which was negative. He continued treatment, but did not improve. On May 20, the visible peristaltic waves were more prominent and he complained of colicky pains in the lower abdomen with distention. An exploratory operation was advised, as a tumor of the small intestine

was suspected, due to the mild obstructive symptoms. One week later, on June 6, 1937, he became suddenly ill with severe pains throughout the abdomen. Examination revealed a board-like rigidity with tenderness throughout. He was sent immediately to the Columbia Hospital. His temperature was 101, pulse 125, and blood pressure 110/62. The white blood cells were 7,500, with 84 per cent polynuclears. A preoperative diagnosis of perforated duodenal ulcer was made, and that afternoon he was operated upon by Dr. George Bunch. There was a segment of the upper jejunum that was red and congested with the omentum partially adherent on one side and an acute perforation of an antimesenteric ulcer about eight inches below the ligament of Treitz. The peritoneal cavity and the pelvis contained a ropy mucoid exudate. The ulcer was infolded with interrupted linen sutures and a tag of free omentum unattached was sutured over the closure. A large drain was inserted and the wound closed.

During the postoperative period the distention was relieved by a Levine tube for five days, and he was given glucose intravenously and by hypodermoclysis daily. At the end of six days he was placed on an ulcer regime and left the hospital on July 10. He continued to improve and has not had any symptoms of importance since. On August 1, 1938, the jejunum was thoroughly studied by fluoroscopic and x-ray examination and showed no evidence of the ulcer or any narrowing. In March, 1939, a similar study was made, which was negative with a normal emptying time of the stomach and jejunum. At this time his spleen was palpable and liver edge was one finger's breadth below the costal margin. An x-ray of his lungs and an electrocardiogram were also negative. When last seen on September 11, 1939, he was still in fair health. The spleen was now moderately enlarged and he was mildly anemic. At that time I was unable to account for the splenic enlargement.

It seemed important to keep this condition in mind when dealing with abdominal symptoms; to separate ulcers of the jejunum without any apparent cause from ulcers occurring in the jejunum with additional ulcers in other parts of the intestinal tract, as found in the enteric fevers, dysenteries, tuberculosis and syphilis; and as an aid in diagnosis, the case emphasized the need of more frequent use of serial x-rays and the 5-hour opaque meal fluoroscopically in the nonperforated cases and the roentgenogram in the erect position when perforation is suspected.

Subsequent Course.—The patient continued to have pains in the lower abdomen and never regained his good health. The spleen remained very large and the liver was palpable two finger breadths below the costal margin. In November, 1939, he began to have a slight temperature and was advised to have another operation to see what could be done. On December 2, 1939, he

Fig. 1
Area of the ulcer as it appeared at autopsy February 17, 1940. Healing is complete with marked fibrosis.

Fig. 2
Posterior aspect. Shows a marked fibrosis with some narrowing at site of previous ulcer.

was admitted to the hospital and the operation was performed on December 8. A small amount of straw-colored fluid was present and the area of the old ulcer was smooth, free of adhesions and entirely healed. About ten inches below this area the intestine had a tuberculous appearance and the mesenteric and retroperitoneal lymph nodes were enlarged. The spleen was enlarged. A lymph node was removed, which, on microscopic examination, showed an inflammatory process only with no evidence of tuberculosis or malignancy. After the operation he ran a temperature daily from 100-101 degrees and gradually grew weaker. Ascites developed and he died on February 17, 1940.

The autopsy was performed by Dr. H. H. Plowden, Pathologist, and his report follows:

This was the body of a white man approximately 60 years of age, well developed, and exhibiting an extreme grade of emaciation. There was a marked distention of the abdomen, and all the tissues were excessively pale in color.

On opening the abdominal cavity there was an immediate escape of a tremendous quantity of clear pale grayish yellow fluid. This fluid amounted to approximately 500 c. c. The peritoneum everywhere, both visceral and parietal, was entirely free of tubercles or tumors. The liver was approximately two-thirds of the normal size and its surface was somewhat wrinkled and irregular in outline. There was a moderate thickening of the capsule and there were a number of adhesions between the liver and the gallbladder and the duodenum and the anterior abdominal wall. The omentum was attached to the inner surface of a fairly recent surgical operative wound of the anterior wall.

Fig. 3

Primary carcinoma of the jejunum. This was located ten inches below the site of the ulcer with perfectly healthy gut in between (autopsy).

At approximately four inches from the upper end of the jejunum there was present an old fibrous tissue band which extended entirely around the circumference of the gut. This was stiff and resistant and on the mucosal surface on the posterior wall of the gut there was a lapping or puckering of the mucosa, with the long end of the pucker extending downward along the lumen of the gut, in such a way as to suggest the possibility that beneath it may have been an ulcer, although definite presence of an ulcer could not be determined grossly. Approximately 10 inches below this point, there was another area of disease of the gut wall, while the intervening 10 inches of the gut wall was quite normal in appearance. This area of disease was itself approximately 8 inches in length, and consisted of a tremendous thickening of the intestinal wall, and the thickening apparently originated in and from the mucous membrane. This and the thickening were of an infiltrative character and involved all layers except the outer serous layer. This was grossly a malignant process, and there were several areas of superficial or mucosal destruction. This area of the gut was thick, tough, leathery and had caused a total obstruction of the lumen of the gut. In connection with this tumor there were found three rounded very minute nodules in the liver substance. They each measured approximately ⅛ inch in diameter. Other similar metastatic lesions were not found elsewhere in the body.

The lungs throughout were soft, crepitant, light in weight, free of areas of tumors, tubercles or areas of consolidation. No pleural adhesions were present. The heart was remarkably small, soft, flabby, and of a pale brownish color. Coronary vessels were prominent, thick, tortuous, somewhat stiffened. Valve leaflets and orifices were normal in appearance. The aorta was thin, slightly dilated and there was slight loss of normal elasticity.

The diagnosis was malignancy of the jejunum with obstruction of the intestinal lumen, minute metastasis in the liver, moderate portal cirrhosis and ascites.

Following is a report of the microscopic sections of tissue removed at autopsy.

Microscopic sections removed from the site of the original operation on the small intestine show a great deal of hypertrophy of the musculature of the intestinal wall, with considerable fibrosis. On the mucosal surface there is present a small chronic ulceration of non-specific character. There is no evidence of malignancy in these sections, and there is no evidence of tuberculosis or other specific inflammatory process.

Microscopic sections made from the tumor of the intestine show a widespread infiltration of the intestinal wall, and practically complete destruction of the whole architecture of the gut wall, except the outer serous covering, by a tumor made up of small irregularly shaped cells which obviously originated from the mucous membrane.

The diagnosis is carcinoma of the small intestine.

Primary jejunal ulcer and primary carcinoma of the jejunum are both extremely rare. The appearance of both as entirely separate diseases

in the upper segment of the jejunum is, I believe, unique in medical literature.

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DISCUSSION (*Abstract*)

Dr. George H. Bunch, Columbia, S. C.—I shall discuss some phases of the surgical problem presented in the case of acute perforation of primary jejunal ulcer upon which I operated for Dr. Zemp and which is the basis of his scholarly paper.

Before operation, if the symptoms are not sufficiently marked to enable one to be reasonably sure of an acute perforation of a peptic ulcer, it is our practice to have a roentgenogram made with the patient in the upright position, to learn if there is free gas under the diaphragm. In this patient this was not necessary, for the symptoms of perforation were classical: sudden severe pain, followed by marked rigidity of the abdominal muscles, fever, and high polymorphonuclear count.

A half hour before operation for acute perforation, we give by mouth, through a glass tube (to prevent discoloration of the lips) methylene blue solution, made by dissolving a one-grain tablet in two ounces of sterile water. On opening the abdomen, the bluish discoloration of the escaping solution, by graphically marking the site of perforation, saves time and reduces to a minimum the necessity for visceral manipulation in a desperately ill patient.

From irritation of the peritoneum by the acid in the fluid which escapes through an acute perforation of a gastric or a duodenal ulcer, the consistency of the exudate which is found in the peritoneal cavity at operation, after perforation, is almost pathognomonic. It is viscid and ropy, and differs from the exudate found in acute appendicitis or diverticulitis. In operating for appendicitis, if the exudate is viscid, the stomach and duodenum should be explored for ulcer and acute perforation.

In Dr. Zemp's case the exudate being viscid, and the symptoms classical, although no ulcer was found in the stomach or duodenum, we felt there must be an acutely perforating ulcer somewhere in the upper alimentary tract. Further search revealed a perforation in the upper jejunum sufficiently high for the acidity of the intestinal contents not to have become neutralized by the alkaline bile, as was also the condition in a previous case seen by us in which a duodenal ulcer below the ampulla of Vater had perforated into the lesser peritoneal cavity.

At operation, except for an edematous congested portion of jejunum about six inches long which began several inches below the ligament of Treitz, the intestine appeared to be normal. On the antimesenteric part of the diseased, indurated segment there was an ulcer with a large perforation. Because of the age and the precarious condition of the patient, we were content to close the perforation with interrupted sutures of fine linen, reinforced by a piece of detached omentum. We were severely tempted, however, to remove by resection the entire segment of intestine with the acute enteritis. This would have removed the pathologic tissue and insured the patient a permanent cure if he had survived the operation. We think that the subsequent history of the case, as given by Dr. Zemp, has justified the safer, more conservative operative procedure which we took.

The case has taught me the necessity of finding the ulcer and closing the perforation when the clinical and the operative findings point to perforation even though no lesion is found in the stomach or the duodenum.

Dr. Cecil O. Patterson, Dallas, Tex.—Dr. Zemp has emphasized the obscure and highly fatal character of primary jejunal ulcer. Richardson has said that this condition is "obscure both in etiology and diagnosis, not hard to overlook on the operating table, and dangerous to life." This affection of the jejunum is rare, it is true; however, in the differential diagnosis, and not uncommonly encountered, are a surprisingly large number of conditions producing similar symptoms and located in the jejunum, as, for example, anomalies of rotation, constricting bands and membranes, diverticula, benign and malignant neoplasms, specific and nonspecific granulomata, intussusception, volvulus, fistulae, and disturbances of motility associated with deficiency diseases. Thus, with an otherwise normal gastro-intestinal tract, even in the light of the best methods of study of the stomach, biliary tract, duodenum and colon, and even though the duodenal bulb and terminal ileum appear normal, there is still, in the presence of suspicious sypmtoms, the obligation to make a detailed study of each coil or jejunum and upper ileum before it can be truthfully said that the digestive symptoms are not due to intrinsic intestinal disease.

Dr. Zemp's patient had nine years of recurring upper abdominal symptoms. Eleven cases of those reported, presented over periods of years recurring symptoms of intestinal obstruction and strictures of the jejunum were found at the sites of the ulcers. With newer methods of study of the physiology of the small intestine, as described by Miller, Abbott, Pendergrass, Barker and Hummel, Peters, Ivy, Snell, and others, disclosing disturbances in ion concentration, in vitamin K absorption, in the general body metabolism of sodium, potassium and calcium, and a consideration of the anemias, these long-standing, partially and chronically obstructing lesions of the jejunum assume ever-increasing importance. Such studies are removing increasing numbers of patients from their former realm of functional indigestion.

Furthermore, in the presence of such common symptoms as constipation and upper abdominal distress of

various types, a careful study of the jejunum is justified, because the patients with a pre-perforation diagnosis and operation for jejunal ulcer had a 12.5 per cent mortality, as compared with the 68.4 per cent mortality in the perforated cases reported; in other words, the patient's chance of survival is almost tripled by a pre-perforation diagnosis and operation.

Dr. J. Shelton Horsley, Richmond, Va.—I should like to call attention to a little monograph by Chester Jones, of Boston, in which he made some interesting observations on this lesion. Dr. Jones found experimentally and clinically that in lesions of the upper jejunum the referred pain is rather constant high in the epigastrium a little to the right of the midline, and is usually accompanied by backache. He also reported a case of duodenal ulcer in which there was backache on both sides. This latter case was treated for a sprained back for some time until finally he was operated upon and a definite diagnosis was made, and he was cured by medical treatment. The etiology of the condition is entirely theoretical. It is probably due to the rapid emptying of the stomach or possibly a relaxation of the sphincter which allows the gastric contents to reach the jejunum before they have been sufficiently alkalinized.

The enteritis described was probably secondary.

Certainly cases have been reported in which ulcers in the jejunum seemed to be the initial lesion and the enteritis described is probably a residual lesion.

Dr. George H. Bunch, Columbia, S. C.—The findings of our case at operation were those of segmental enteritis. I think the ulcer and the perforation were secondary to this.

DERMATOMYOSITIS IN CHILDREN*

A REPORT OF TWO CASES WITH A FATAL TERMINATION

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and
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Brock[1] stated that our conception of dermatomyositis would be materially clarified

"If it is understood that dermatomyositis is nothing more than a non-purulent, non-hemorrhagic type of polymyositis in which there is, in addition, an inflammation of the skin."

The first recorded case of dermatomyositis was described by Wagner[2] in 1863, under the title of "A rare muscular disease." In 1887, the condition was carefully described by Wagner,[3] Hepp,[4] and Unverricht.[5] Unverricht[6] was the first to call this syndrome dermatomyositis.

We wish to report two cases occurring in children with a fatal termination. The literature has been well reviewed by Marcus and Weinstein,[7] Lane,[8] Karelitz and Welt,[9] Wheeler and Harbin,[10] and others.

Few cases in children have been reported in the American literature. It occurred to us that the presentation of two additional cases in children might result in a discussion that would contribute to a more rational therapeutic approach to this interesting disease. We have reviewed the case reports in children by Steiner,[11] Moore and Koch,[12] Karelitz and Welt,[9] Sydenstricker and Thomas,[13] Saunders,[14] Rudolph,[15] O'Leary,[16] Dennis,[17] Wheeler and Harbin,[10] Blumenthal and Pinkus,[18] and Turner.[19]

CASE REPORTS

Case 1.—A. H., a seven-year-old school girl, was first seen in the pediatric outpatient department March 30, 1938, and admitted to the hospital with a diagnosis of acrodynia. Her mother gave for her a history of an erythema and edema of the eyelids, face, hands and feet, of six months' duration. Soon after the onset of the skin manifestations the patient complained of pain in her legs when she reached home from school. The edema and pain increased in such severity within a period of three weeks that she was unable to attend school.

She was put on a high vitamin diet and made considerable improvement during the summer and fall of 1938.

On December 5, 1938 she was seen again with a marked recurrence of symptoms and increased weakness. There was a dullness in the left upper chest and intense pain over the large muscle groups. Examination by one of us revealed a markedly emaciated seven-year-old girl. There was a non-pitting edema of the face, neck, and extremities, and a purplish, scaling, macular eruption over the face, arms, forearms, hands, and lower extremities. The skin over the large joint surfaces was atrophic, and a shiny red color. The pain over the muscle groups was so intense that the slightest palpation caused the patient to cry out with pain. The skin in addition to the scaling eruption showed many areas of depigmentation and hyperpigmentation, and large areas excessively moist with perspiration. The hands were of particular interest in that the fingers showed a scleroderma-like edema. Over the distal portions of the fingers there was a deep erythema not unlike that seen in cyanosis. The fingers had a tapering appearance and over the dorsum and fingers and over knuckles of the hands there were multiple white nodular swellings, many of which were blue in the center, and others were ulcerated in a manner resembling ecthyma. There was considerable muscular wasting in the first intra-osseous spaces. There were similar ulcerations of the skin over the shoulders and the region of the posterior surface of the shoulder joint and over both elbows. The muscles of the shoulder girdle group showed marked atrophy and the patient was unable to

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*Read in Section on Dermatology and Syphilology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

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hold a glass of water. The forearms were slightly flexed upon the arms.

The heart was markedly enlarged and a diffuse apex beat was palpable posterior to the posterior axillary line. A soft systolic murmur was heard over the whole precordium. The blood pressure at rest was 80/30, and the pulse rate was 120, and the temperature 98.2. Twelve teeth showed marked caries. The tonsils were slightly enlarged and the pharynx was more red than normal. Examination of chest revealed dullness over the lower left chest anterior and posterior. There were coarse rales over the left apex. The spleen was palpable.

Laboratory findings on admission were: hemoglobin, 95 per cent; red blood cells, 3,000,000; white blood cells, 9,000; and the differential count was normal. The blood Wassermann was negative. The nonprotein nitrogen was 44; urea, 44; creatinin, 1.7; blood sugar, 81.6; blood chlorides, 396 mg. per cent; blood cholesterol, 58.8; blood calcium, 9.5; vitamin C in the blood, 1 mg. per cent. Urine was normal except for a trace of albumin. The sputum contained long chain streptococci, gram negative and gram positive diplococci. The tuberculin skin tests were negative. The basal metabolic rate was minus 15. Electrocardiogram showed right axis deviation and indicated a toxic myocarditis. Roentgenograms of the chest showed the heart to be markedly enlarged, mainly to the left, with very shallow excursions of the heart border. There was infiltration in the upper left lobe, which was almost completely obliterated by the heart.

A diagnosis of dermatomyositis was made from a memory of similar cases described in the literature.

It was advised that the patient be put on a high vitamin diet, with large doses of vitamin C and vitamin B being administered by mouth and hypodermatically.

The course in the hospital was uneventful with some suggestion of improvement until December 27, twenty-two days after admission, at which time the patient developed an acute tracheobronchitis. Her temperature at that time was 103.2 and the patient was acutely ill. There were moist rales heard throughout the chest. The pulse rate was 150 and respiration 48. A diagnosis of bronchial pneumonia was made. Large doses of sulfanilamide were administered intramuscularly. She had great difficulty in swallowing. There was very little excursion of the chest on respiration. She was given blood transfusions, fluid intravenously, but her condition became progressively worse, and on January 9, fourteen days after the onset of the pneumonia, the patient died. Autopsy studies were not obtained.

PATHOLOGIC REPORT

Skin Biopsy.—The skin is remarkably thin and in places not greater than two or three cells in thickness. The border of the cutis is very irregular but in no place can a layer be found which corresponds to the normal thickness of the skin. The papillary bodies in some places are swollen and widened and show a proliferation of cells in the upper portion. The widening

Fig. 1, Case 1
Atrophy of shoulder girdle muscles. Erythema and ulceration over bony prominences.

Fig. 2, Case 1
Erythema and edema of the hands: Firm, white nodular swellings over knuckles.

and enlargement is apparently the result of edema. The upper portion of the corium is thickened with connective tissue and elastic fibers. Some of the collagen fibers are swollen. Sweat glands are rather abundant. Many of the connective tissue cells, especially deeper in the corium, show cloudy swelling and early degeneration. Below the corium there is fat in the connective tissue. Many of the fat cells are atrophied. A few of the small blood vessels within the fatty tissue show a perivascular infiltration of mononuclear leukocytes. The connective tissue surrounding fat globules shows evidence of early degeneration and edema. Throughout the corium the small capillaries show perivascular infiltration of leukocytes of the monocytic type. There is an increased amount of keratin material covering the cutis. A few of the epithelial cells, especially in the germinal layer, show vacuolization of the cytoplasm. The papillary bodies are infrequent with a tendency to be flattened out or absent. Many of the small capillaries show a proliferation of the lining endothelium. Some of these endothelial cells have migrated out into the loose connective tissue surrounding the capillaries. The cytoplasm of the lining endothelial cells is swollen which considerably narrows the lumina. The arrectores pilorum show early degeneration changes chiefly in the form of pale-stained muscle cells many of which show vacuolization of the cytoplasm. Many of the nuclei are disintegrated. A few of the cells are edematous and show cloudy swelling.

Muscle Biopsy.—Cross sections and longitudinal sections of small fragments of muscle show considerable muscle atrophy. Many of the muscle cells stain very poorly and show a vacuolization of the cytoplasm. Numerous nuclei show various stages of degeneration. Striation in the degenerated fibers have disappeared. In between many muscle fibers there is an accumulation of monocytic leukocytes. Some of the muscle fibers present a wavy appearance. Many of the blood vessels, including the small capillaries, are greatly congested. Various sections present a very cellular appearance due to muscle atrophy in which the nuclei lie more closely together. In some parts there appears to be slight edema.

Microscopic Diagnosis.—The histologic findings are all characteristic of dermatomyositis. The changes in the skin, the muscle degeneration show all of the features which have been described in these tissues in this disease.

Case 2.—I. D., an eleven-year-old school girl, had had many childhood diseases in her early life and did not walk until the age of four. Eight months previous to hospital admission, she had a purplish colored, scaling eruption over the face, neck, and extremities. She had a low-grade temperature and occasionally had chilly sensations and excessive perspiration. Three or four months following the appearance of the skin lesions she began having pain in the muscles. She was seen by the pediatric department and the diagnosis was deferred. She was admitted to the hospital for study on October 18, 1938. Eight days later she was seen by one of us, at which time she was acutely ill. The face was so edematous and the upper eyelids so swollen that the patient was scarcely able to open her eyes wide enough for any vision. The skin showed a dark erythema over the face, neck, extremities, buttocks, and abdomen. There was a maceration of the skin in the folds of the neck, axilla, and decubitus type ulcerations over the shoulders and buttocks. There was a marked hyperpigmentation and depigmentation of almost the entire skin surface. The forearms were almost completely flexed upon the arms, and the legs upon the thighs, and could not be extended. The slightest movement of the body caused the child to cry out in pain. There was a marked atrophy of the muscle groups which could be felt through the rather diffuse, nonpitting edema of the subcutaneous tissue. The hair over the posterior portion of the scalp was very scant. The mucous membranes of the mouth and gums were spongy and bled easily. The teeth were carious and the tonsils enlarged. There was so much difficulty in swallowing that only sips of fluids could be taken. The excursion of the chest was so shallow that it was difficult to see any motion of the chest wall. Examination of the heart showed a definite enlargement and a roughened systolic murmur at the apex. Musical rales and considerable dullness of the chest were found. Temperature was 103.8°; respiration, 40; pulse, 140. The spleen was easily palpable.

Hemoglobin was 75 per cent; red blood cells, 4,000,000; white blood cells, 11,000; differential count was normal except for 6 per cent eosinophilia; the blood Wassermann was negative; nonprotein nitrogen, 30.6; creatinin, 1.3; blood sugar, 86.9. The urine was normal. The gastric analysis showed an absence of free hydrochloric acid. Total protein of the blood was 9.28; albumin, 5.18; globulin, 4.10. Roentgenograms showed irregular spotty infiltration in the upper right lobe, lower inner zone, and left hilus, suggesting a bronchial pneumonia. The sella turcica was normal. The joint spaces of both knees were narrowed and there was marked decalcification of the adjacent bones. The vitamin C content of the blood showed 1.2 mg. per cent. Electrocardiogram showed toxic myocarditis.

A diagnosis of dermatomyositis complicated by bronchial pneumonia was made. The patient was imme-

Fig. 3, Case 2
Contracture of extremities. Edema of the neck and decubitus ulcer over the buttocks.

diately put on sulfanilamide intramuscularly, vitamin B_1 parenterally and small transfusions. She grew progressively worse and expired on October 31, thirteen days after admission. Autopsy studies were not made.

PATHOLOGIC REPORT

Skin Biopsy.—Sections from various parts of the biopsy material show the skin in a rather advanced stage of degeneration. Here the cutis is extremely thin and the papillary bodies have almost entirely disappeared. The upper portion of the corium is greatly thickened with fibrous connective tissue which also shows various stages of degeneration. Sweat glands, hair follicles and sebaceous glands are very scanty. There is a marked amount of edema which involves particularly the corium and subcutaneous tissues. In the upper portion of the corium there are scattered areas of necrosis in which many connective tissue cells have completely disintegrated and are replaced by leukocytes, chiefly lymphocytes which are mixed with the remaining debris. Elastic fibers are swollen. The fat in the subcutaneous tissue was also involved in the degenerative process as shown by disintegration of connective tissue throughout the fat and around the fat globules. In many fat cells and collagen fibers the

Fig. 4, Case 2
Scanty hair over the scalp and non-pitting edema of the neck. Erythema and disturbance of pigmentation.

Fig. 5, Case 2
Erythema, edema and scaling of the eyelids. Prominent hair follicles over hands and wrist.

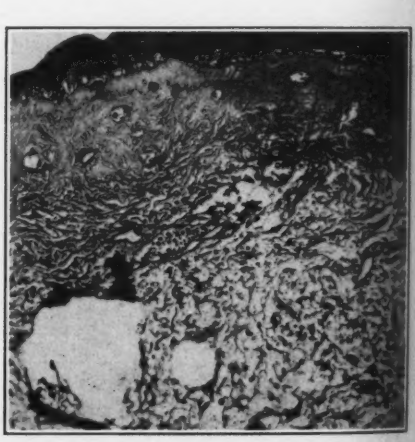

Fig. 6, Case 2
Edema and degeneration of corium. Area of dense fibrosis, left upper corium. Advanced degeneration of epidermis over area of fibrosis.

nuclei are degenerated. Around the tips of some of the hair follicles there are many scattered lymphocytes. In the germinal layer of the epidermis the majority of cells are degenerated; at least one-third contain vacuolized areas in the cytoplasm. The nuclei in many of these cells show disintegration and the keratin of the surface is moderately thick and compact. Most of the small blood vessels are congested and there is slight perivascular infiltration of some of them.

Fig. 7, Case 2
Frayed, degenerated muscle cells. Edema and Zenker's hyalinization. Interruption in continuity of fibers.

Fig. 8, Case 2
Hyperkeratosis. Thinning of epidermis and disappearance of rete pegs. Hydropic generation of germinal layer, edema, endothelial proliferation of capillaries in corium.

Muscle Biopsy.—The muscle stain is very pale, but the changes are similar in every respect to the changes observed in the preceding case. The muscle involvement, however, is not quite so severe and there are not so many leukocytes between muscle fibers and muscle bundles.

The microscopic diagnosis is dermatomyositis.

PATHOLOGIC SUMMARY

The histopathologic changes in both cases are strikingly similar and particularly characteristic and in keeping with the findings of biopsy studies reported by other investigators. As regards the cutis, it is definitely thin and the germinal layer appears to be involved to a great extent; the papillary bodies become small and the base levels off until the epidermis becomes a very smooth, regular layer (*Fig. 9*). In both cases the papillary bodies have become very scanty and tend eventually to disappear. The germinal cells show a definite tendency to early degeneration by the appearance in the cytoplasm of vacuolated areas. The nuclei become granular and disintegrate (*Fig. 10*). In many places the epidermis will not be more than two or three cells in thickness. The keratin layer becomes thickened and more compact. Hair follicles and sebaceous glands show the effect of degeneration. The sweat glands, however, appear to be the least affected and even in the advanced stages most of these glands appear to be healthy. In some sections

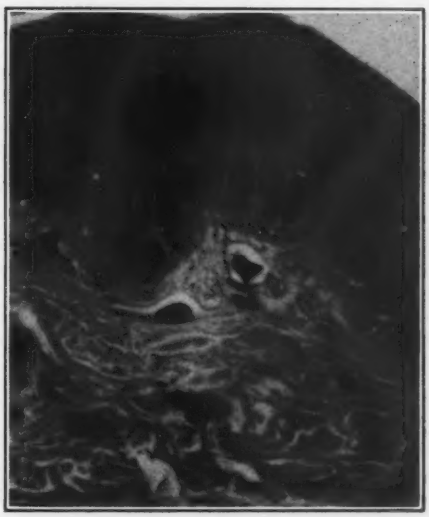

Fig. 9, Case 2
High power of Fig. 8. Hydropic degeneration in cell nuclei.

they stain a brilliant color. The cytoplasm of these cells is large and they show every evidence of activity and physiologic function. The corium thickens with connective tissue and elastic fibers, particularly the latter, which also show the effect of the degenerative process by gradually swelling and the distintegrative formation of cellular debris (*Fig. 11*). The fatty tissue also becomes involved in the degenerative process. In general the subcutaneous tissue including the corium does not show the usual lymphocytic infiltration that we find in scleroderma, but there is much fibrosis particularly of the upper corium. The rete pegs are greatly diminished in dermatomyositis (*Fig. 12*). From a study of these and other cases of dermatomyositis, poikilodermia, and scleroderma, we find clinical and pathologic features that are common to each, and as more cases are studied and reported we may observe a closer relationship of these three interesting diseases.

CLINICAL COMMENTS

These cases presented the cardinal symptoms that have been reported in similar cases. Both showed definite pigmentary disturbances with hyperpigmentation and depigmentation. This manifestation has not been extensively discussed either as to significance or etiology, except by Talbott[20] and his co-workers who in a similar case were inclined at first to make a diagnosis of Addison's disease. The outcome was fatal as it is in so many severe cases involving the muscles of swallowing and respiration. Bronchial pneumonia, a complication resulting from inadequate aeration of the lungs, was the cause of death in both cases. The toxic myocarditis was present in both cases and at first suggested pericarditis with effusion.

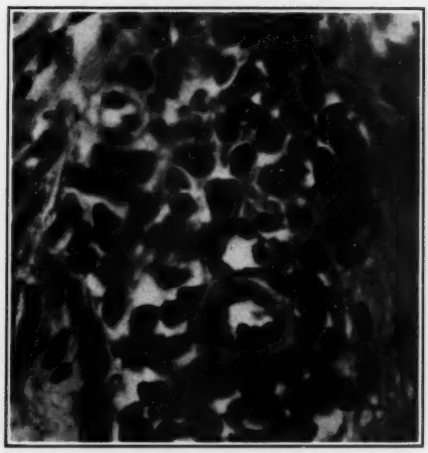

Fig. 10
Marked monocytic proliferation in the corium. Endothelial and large monocytes predominating.

Fig. 11
Marked hydropic degeneration of arrectores pilorum. Nuclear disintegration.

Fig. 12
Extensive hydropic degeneration of muscle cells. Fraying and interruption of continuity of muscle fibers.

ETIOLOGY

The etiology has remained obscure. Bacterial infection has been regarded as the cause by the majority of workers. Grunke[21] regarded tuberculosis as a cause in his reported case. Rosenow isolated streptococci from the muscle of one of Brock's[1] cases, and a diplostreptococcus from biopsy tissues in another case reported by Brock. Vitamin deficiency also has been considered as an etiologic factor by Guy.[22] Marinescu[23] and his co-workers believe that dermatomyositis is due to a filterable virus, similar to that which has been demonstrated in periarteritis nodosa, with a special affinity for connective tissue and vessels. Greenaway and Lambie[24] believe that the muscles are primarily affected and that as a result a substance develops which renders the patient sensitive to light, and that the cutaneous lesions are secondary manifestations due to photosensitivity. Greenbaum[25] suggests that "It is possible that the etiologic factors connected with lupus erythematosus are similar to those connected with dermatomyositis." He also feels that sun rays are definitely an exciting factor which produces a kind of trauma, elaborating or provoking a cutaneous lesion, but there must be an associated endogenous factor, probably a toxin, which determines this reaction. Lane[8] feels that there is a very close resemblance between acute cases of dermatomyositis and acute cases of lupus erythematosus disseminata. He is also of the opinion that the etiologic factors may be the same. We feel that the etiologic factor is most probably a toxin which may result from many different types of infection rather than actual infection in the muscles and cutaneous structures. The pathologic studies of the muscle tissue tend to confirm this attitude inasmuch as the cellular infiltrate is almost exclusively lymphocytes. The areas of necrosis, edema and atrophy reveal little, if any, evidence of cellular or vascular reaction which would characterize an inflammatory process.

TREATMENT

In dermatomyositis there are definite instances of remissions and in some instances apparently complete recovery. This makes the evaluation of any treatment difficult. In the severe cases, particularly in children, in which the muscles of respiration and swallowing are involved, the treatment has been almost universally unsuccessful. O'Leary[26] has suggested the use of oxygen, either by means of the oxygen tent or through the nasal tube, typhoid vaccine, either subcutaneously or intravenously, and glycine. Dennie[17] has also recommended typhoid vaccine. Others have used glycine and high vitamin diets. Hopkins[27] used glycine and prostigmin, and in one case its use was followed by marked improvement, but the patient later died. Should the treatment of oxygen recommended by O'Leary have a rational basis, and well it may, since there is a great reduction in the vital capacity of the lungs, the use of sulfanilamide would be contraindicated. It occurs to us that adrenal cortex would be a logical therapeutic agent, since in our cases there was so much disturbance of pigmentation, which may or may not have been related to adrenal insufficiency. This thought could be further justified, since it is well known that in tissue destruction there is an escape of potassium ions from the cells into the blood stream. The increased blood potassium may act as a toxic agent. Talbott[20] found a negative sodium and chloride balance in his case of dermatomyositis associated with marked pigmentary disturbance. There is against this premise the fact that he did not find any pathology in the adrenal cortex at autopsy. Campbell[28] has shown that there is an adrenal insufficiency in cases of bromide psychosis and in bromoderma. He states that there is a loss of blood chlorides with a replacement of bromides, and that the administration of adrenal cortex dramatically restores the blood bromides to normal and that the toxic symptoms disappear after twenty-four to forty-eight hours. Moderate fever therapy is apparently a rational treatment, since it produces an elevation of the basal metabolism, an increase in blood pressure, dilatation of the small blood vessels, and an increase in the aeration of the blood in the lungs, and promotes the elimination of toxic products. It may also act in some nonspecific way.

We feel that oxygen and helium should have a definite place in the treatment of the acute symptoms which arise from respiratory embarrassment and result in marked cyanosis prior to the fatal termination. Glycine and prostigmin as used by Hopkins have been used in Dercum's disease, which is characterized by painful subcutaneous nodules involving the fascia of muscle groups.

Turley and co-workers[29] and Sulzberger and co-workers,[30] working independently, have shown that histamine will change lymphocytes into eosinophils when added to washed cells. This changes our conception of their formation. It leads us to believe that in certain toxic states

histamine may produce histologic changes that have not before been explained. Dale[31] has proven the action of acetyl choline in nerve impulse and the production of a histamine-like substance at the nerve endings in response to the release of acetyl choline. There is also an enzyme liberated which limits the extent of the histamine-like reaction. It occurs to us that in those cases which exhibit a high eosinophilia, this mechanism may be the explanation. Should this premise be true, it would suggest the use of the enzyme histaminase.

DIFFERENTIAL DIAGNOSIS

The most difficult problem is to distinguish dermatomyositis from early cases of acute scleroderma of the diffuse type. Allan[32] considers the symptoms and clinical course of both conditions practically the same and believes that the difference lies more in the observer. In diffuse scleroderma there is more perivascular infiltration in the corium. Brock[1] states that in diffuse scleroderma there is less muscular degeneration and lymphocytic infiltration and that the pathology found in the muscles is more of a subsequent myosclerosis than a myositis.

Dowling and Freudenthal[33] consider poikiloderma to be similar to dermatomyositis in many ways. In their excellent article they give a table of clinical and histologic differences. We have had an opportunity to study the two diseases concurrently in the hospital, and we consider poikiloderma to be a probable reticuloendotheliosis.[34] The skin lesions in poikiloderma show a marked cellular infiltrate in the corium and resemble healed radio dermatitis clinically; the disease is more chronic and often terminates with some form of lymphoblastoma.

Dermatomyositis must be differentiated from trichinosis. Roentgenograms in cases of trichinosis reveal the calcified encysted larvae. Histological study of muscle tissue shows many larvae. There are more gastro-intestinal symptoms early and the leukocytosis is more marked in trichinosis.

Lupus erythematosus disseminata may resemble dermatomyositis. It usually is accompanied by a leukopenia and the muscles do not show degeneration and atrophy. A diagnosis of acute lupus erythematosus disseminata is made more easily if there is a history of chronic discoid type lesions.

The question of what constitutes the differential diagnosis between dermatomyositis and poikilodermatomyositis may well arise. In 1905 Petges and Clejat[35] described an affection which they called "atrophic sclerosis of the skin and generalized myositis." In 1908, Jacobi[36] described "poikiloderma atrophicans vascularis." In 1929, Petges, convinced that his first case and several others that he had observed were related to Jacobi's disease, changed the name to "poikilodermatomyositis." This name brought dermatomyositis and poikiloderma atrophicans vasculare into one group. We think that Jacobi described a case of burnt-out dermatomyositis and agree with Dowling and Freudenthal[33] when they speak of the "Lane" type of poikiloderma atrophicans vasculare. We consider the use of the term "poikilodermatomyositis" unfortunate unless one wishes to describe a chronic phase of dermatomyositis.

SUMMARY AND CONCLUSIONS

Two cases of dermatomyositis in children with fatal termination are reported.

These cases presented similar involvement of the skin, muscles and heart.

The rationale of adrenal cortex, helium and oxygen, histaminase, and fever therapy is presented.

The problem of differential diagnosis is discussed.

A brief review of the literature is given.

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DISCUSSION (*Abstract*)

Dr. Charles O. King, Birmingham, Ala.—The American literature contains reports of comparatively few cases of dermatomyositis in children. Drs. Hazel and Hull are to be commended on seeing and recognizing and reporting these two rare cases in one city in the same year. In the past fourteen years, I have seen only two cases which were recognized.

Both of their cases present the cardinal symptoms of the syndrome as reported in the literature: swelling of eyelids, erythema, edema, pains in the joints and muscles, extreme weakness, vascular and pigmentary disturbances as depigmentation and hyperpigmentation; excess perspiration and later fixation and contractures of limbs, one of these, atrophy of the girdle muscles.

It was Osler who said that dermatomyositis was, after all, a deep-seated scleroderma and the fact that these two, as well as poikiloderma, have so many symptoms in common makes one wonder if after all the same process is at work and eventually that they will all be classified as the same disease. It is true that in poikiloderma the face is spared usually. From the description in the literature it is sometimes very difficult to distinguish between the two. The contrast is striking when they are seen side by side on account of the lack of involvement of the face.

Generalized diffuse edematous scleroderma at onset is apparently cutaneous and subcutaneous and sometimes muscular, whereas dermatomyositis is fundamentally always muscular.

In some cases of dermatomyositis the course is limited as in scleroderma, while in other cases the process will go on to calcinosis or death.

Some writers are decided that the cause of these is a definite infectious process. The streptococcus has been demonstrated early in the process, but seldom found late.

Both of the cases demonstrated had carious teeth and seemingly infected tonsils. There is a possibility that the infectious process begins in either of these areas. Yet, the cause of this entity seems still to be obscure.

The histologic changes in both are striking and well pointed out in this paper. I want to commend these gentlemen on the enormous amount of time and energy spent on this entity.

Dr. L. C. Sanders, Memphis, Tenn.—I am an internist and know very little about dermatology. However, ten years ago it was my privilege to study a patient with dermatomyositis, and I shall mention very briefly a few features of this case.

My patent was a girl 11 years old. She had been ill for three months when I saw her. She had a cherry red rash on the face and neck, edema of the face and limbs, enlarged infected tonsils, an average temperature of 101° F., masked features, contracture of both arms and legs, wasting of all the muscles and complete loss of muscular control. The laboratory tests were not significant, except for a positive Streptococcus hemolyticus blood culture. In searching the literature at that time I found fifty reported cases, only three of which had had blood cultures done, and none was positive. Microscopic sections of muscle fibers showed the typical degenerative changes reported in similar cases.

In conclusion, I want to say that I had some difficulty in arriving at a diagnosis. The textbooks which mentioned the disease gave such vague descriptions of it that I could get no information of value from them. Finally, I located a case report in one of the journals which gave me a clue, and in searching the literature further I was able to discover about fifty cases recorded.

My patient gradually declined, the muscles wasting almost completely away, so that she became a mere skeleton. Death occurred two years after onset due to respiratory failure.

Dr. Clinton W. Lane, St. Louis, Mo.—This is an important subject, because often clinical resemblance of dermatomyositis to other dermatoses makes difficult a diagnosis in the early stages.

In the first case observed by us and subsequently reported before this Section four years ago, a diagnosis of disseminate lupus erythematosus had been considered. The distribution and color of the eruption, the fever and apparent arthritis made such a diagnosis tenable, but a consulting neurologist discovered that the joint pains occurred only when muscles and tendons were moved or palpated. This case terminated fatally from involvement of the muscles of respiration and pulmonary edema.

A second case, a man, who had always eaten a great deal of pork and in whom the erythema first appeared on the eyelids and face, was at first diagnosed as a case of trichiniasis. This patient developed an acute, extensive dermatomyositis and died within a

few months of respiratory failure and bronchopneumonia.

The third patient was a girl of 11 years, in whom the disease developed subsequent to scarlet fever, and who was also at first diagnosed as lupus erythematosus.

In the fourth case an erythema and edema appeared on the neck and face and by this time we had become dermatomyositis conscious and made the diagnosis. It proved to be a scleredema adultorum of Buschke and cleared up completely in a short time.

In unusual erythemas and edemas of the face and neck, not only lupus erythematosus, trichiniasis, erysipelas, scleredema and acute scleroderma must be considered, but also dermatomyositis. Early diagnosis is important in offering a better prognosis for this disease.

Dr. G. P. Lingenfelter, Denver, Col.—I have seen two cases within the last eighteen months in consultation, in which I made a diagnosis of dermatomyositis. Both of those cases had followed scarlet fever, and I should like to ask Dr. Hazel if there was any history of scarlet fever preceding his cases.

Dr. Hull (*closing*).—In studying the biopsy material with Dr. Hazel of these two interesting cases, a number of pathologic or histologic changes were seen which bear a striking resemblance to two other interesting conditions, namely, scleroderma and poikiloderma. This refers particularly to the corium. In scleroderma the corium is very thick and dense and extends rather deeply into the lower parts of this layer. In poikiloderma the corium is also affected, but more in the upper part, and it is very dense with fibrous tissue and presents more inflammation than either of the two other conditions. In dermatomyositis the corium is also thickened.

There are some interesting features that pertain to the stratum germinativum. First of all, the rete pegs tend to become destroyed in all three conditions and finally the layer becomes very smooth and regular so that it appears to lay flatly on top of the corium. Perhaps as we study other cases and other cases are reported, we shall begin to observe a closer and closer relationship between these three conditions.

I should like to make a point or two about the study of biopsy materials, and that is that we should consider that the skin varies a great deal in its histological structure from one part of the body to another. We should keep in mind the site from which the biopsy is taken and the stage of the disease process, its acuteness or its chronicity, and we should remember that skin conditions vary greatly in the histologic changes in different individuals. The same disease may vary greatly.

What causes this condition? Certainly, the etiology is very obscure and open to wide speculation. We have not been able to connect any definite etiology with our cases, but we speculate a great deal on some of the things that might explain it. First of all, might not the metabolism of the skin be involved? Do the electrolytes accumulate in the skin and what effect would they have if they did? Perhaps as we learn more about the biochemistry of the skin many of these conditions will begin to clear up.

In answer to the question by Dr. Lingenfelter, Case 2 had scarlet fever at the age of 4.

CLINICAL USE OF MALE SEX HORMONE*

A FURTHER REPORT

By HENRY H. TURNER, M.D.
Oklahoma City, Oklahoma

In a previous paper[1] I reported the results of two years' observation of fifty-four patients with various types of genital anomalies and dysfunctions, which included adult hypogonadism, sexual diminution associated with senescence, adiposogenitalism, gynecomastia, and benign prostatic hypertrophy, who were treated with the synthetic male sex hormone, testosterone propionate.† In doses of 10 to 75 mg. weekly, it was found effective in every hypogonad case, as evidenced by promoting hair and penile growth, producing erections and emissions, developing the libido and potentia coeundi, and by generalized changes in secondary sex characteristics. The androgen brought about considerable relief of the subjective symptoms of sexual diminution associated with senescence, and in cases of benign prostatic hypertrophy, as shown by the clinical improvement in the usual symptoms and signs of prostatic obstruction. No untoward by-effects were noted in any of the cases treated.

The purpose of this study is to report the progress of the hypogenital patients of that group and additional ones observed during the past year. The primary treatment consisted of intramuscular injections of 10 to 25 mg. of testosterone propionate dissolved in sesame oil, two to three times weekly, and later the daily percutaneous administration of 2 to 8 grams of the androgen dissolved in an ointment base and containing 2 mg. of the hormone per gram. Response was evidenced by the growth of the penis, increasing libido and potentia coeundi, ejaculations, hair growth, and other signs of sexual maturity.

CASE STUDIES

Case 1.—C. G., aged 40 years, presented a typical appearance of an obese eunuchoid individual. During the years 1933 and 1934 he received a total of 19,200 units of anterior pituitary-like sex hormone ("antuitrin-S") and anterior pituitary sex hormone ("prephysin") with some improvement in his general condition, but no ap-

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*Read in Section on Medicine, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*From the Department of Medicine, University of Oklahoma School of Medicine, and the Endocrine Clinic of the University and State Crippled Children's Hospitals, Oklahoma City.

†Generously supplied for this study by Dr. Max Gilbert, of the Schering Corporation.

preciable objective changes in the genitals, probably because of the small dosage which was customarily given at that time. Injections of 25 mg. of testosterone propionate three times weekly were begun, and after a total of 300 mg. there was obvious growth of the genitals. After eighteen weeks of this treatment the injections were changed to placebo injections of sesame oil, and after about four weeks of this treatment he began complaining that the substance was losing its potency. Sexual desire and ability rapidly decreased, and after six weeks of these placebo injections, testosterone was again prescribed and improvement was immediate. After a total of 2,925 mg., his functions were essentially normal and a small prostate could be felt, but no testes could be palpated, showing no change from the original cryptorchid state. No spermatozoa were found in the ejaculate, which measured 0.6 c. c. The voice deepened remarkably, and the larynx grew to such an extent that it became necessary to increase the shirt size by one-half, even though there had been no appreciable increase in body weight. The blood pressure remained normal at all times, and roentgenograms of the extremities revealed no progress toward epiphyseal closure. In November, 1938, the dosage was reduced from 75 mg. per week to 30 mg. per week, and he progressed satisfactorily. In January, 1939, daily inunctions of 8 mg. of testosterone in an ointment base were prescribed plus one injection of 10 mg. per week. After seven weeks of this combined treatment, he stated there was definite reduction in his libido and potentia, and insisted on resuming the triweekly injections of 10 mg. He recently remarried, and says he has been able to perform his marital duties quite satisfactorily. To date, he has received 4,280 mg. of testosterone propionate by injection over a period of 102 weeks. There has been no further increase in the size of the penis during the past year, and the prostate has increased only slightly. It is well formed, but definitely underdeveloped. He now shaves about three times weekly, whereas formerly he shaved once per month, and there has been appreciable increased hair growth over the extremities, abdomen and the axillae. No spermatozoa have been demonstrated in the ejaculate. His present weight is 235 pounds, which is essentially the same as when treatment was instituted. The epiphyseal line is still evident in the distal ends of the ulna and radius and shows no change from the original x-rays.

Case 2.—S. P., a classical 26-year-old castrate who, during a six-month period in 1936, received 11,500 rat units of anterior pituitary-like sex hormone and during the latter part of this period anterior pituitary-like sex hormone plus anterior pituitary gonadotropic hormone. There was no obvious improvement as a result of this treatment, probably because of inadequate dosage. After sixteen weeks of treatment consisting of 10 mg. of testosterone propionate intramuscularly three times weekly, he had gained 21 pounds in weight, the penis had grown to average normal, and his general appearance and demeanor were those of an average individual. Erections occurred daily, but the ejaculate, amounting to 0.2 c. c. of white viscid fluid, contained no spermatozoa. After a total injection of 1,630 mg. over a period of forty-five weeks, there was increased hair growth over the entire body, the penis was quite normal in size, sexual desires and relations were average. The prostate, which was not palpable at the beginning of treatment, was now about the size of a half dollar, but quite flat and smooth. After a total injection of 2,140 mg. over a period of eighteen months, the treatment was interrupted for twelve weeks, but six weeks after discontinuing the injections he began to notice a very marked decrease in his erectal powers, loss of ejaculations, and decreased libido. It was interesting to note that there was no appreciable decrease in the size of the phallus. Testosterone ointment was prescribed at this time, with instructions to rub in 2 grams nightly, approximately 4 mg. of testosterone. These inunctions were continued over a period of eight weeks. At the end of this time, he stated that he was getting some response from the topical applications, but they were not nearly so effective as the injections. He was then advised to take one intramuscular injection of 10 mg. per week and continue the percutaneous administration of the ointment, in the amount of 4 grams daily. Two months later he reported that he had married since we last saw him and was having very satisfactory intercourse three to five times weekly. To date, he has received a total of 2,260 mg. of testosterone propionate by injection and 300 mg. by inunction, and has developed a normal penis, sex desires and ability which have been maintained during the past four months by weekly injections of 10 mg. and nightly topical application of 4 grams of the ointment containing 8 mg. of testosterone.

Case 3.—M. G., aged 29 years, presented genital hypoplasia. He said that he had had infrequent erections and an occasional orgasm. The examination showed a very thin, undernourished male with the usual disproportion of measurements. There was no facial hair, and he stated that he had never shaved. There was very scant axillary and pubic hair. The penis was quite small. Both testes were descended and well developed. The prostate was small, thin and flat. Findings of blood and urine examinations were normal. Roentgenograms of the skull indicated a small selia turcica, and those of the wrists showed the epiphyseal lines still quite evident. Four years previously he received 1 c. c. of plain anterior pituitary extract ("antuitrin") daily for approximately three months, without any appreciable change in his condition, and some time later anterior pituitary-like sex hormone ("antuitrin-S"), 100 units every other day for a period of two months, which he believed to be of some benefit. Treatment was instituted with injections of testosterone propionate, 10 mg. three times weekly. Following the administration of 180 mg., the libido and potentia coeundi increased. Erections and ejaculations became more frequent. Hair on the pubes became more abundant and the penis and testes increased in size. After eleven months of treatment, total dosage 3,150 mg., the penis had tripled in size and the prostate assumed a fuller normal contour and enlarged to approximately one-half average size for the age. His sex urge and power increased remarkably. Hair on the face and pubes showed increased growth. During the following seven months he received 1,675 mg., partly by injection and occasionally by rubbing in the oily solution. His progress continued satisfactorily. He was then given testosterone ointment, 4 grams to be applied nightly. Three months later he informed me that due to a misunderstanding of directions he had used the ointment only three times weekly. He complained of marked decrease in libido and potency. On 25 mg. per week by injection and 8 mg. daily by inunction during the past two months he has maintained successful sex functions.

X-rays of this patient showed no advancement of epiphyseal union after forty-five weeks of testosterone

therapy. Another film made a few days ago, after a total of 5,055 mg. administered over 102 weeks, was essentially the same.

Case 4.—M. H., a white boy, aged 16 years, complained of obesity and underdevelopment of the genitals. Physical examination showed a typical adiposogenital individual with girdle obesity and rather extreme mons veneris padding. The testes were about normal in size, but apparently fixed in the extreme upper poles of the scrotum. The penis was infantile. A few hairs were scattered over the pubes. Results of routine laboratory examinations were essentially normal.

The first stage of treatment consisted of a prolonged course of injections of the anterior pituitary-like hormones, with complete descent of the testes but without any evident increase in the size of the penis. Injections of testosterone propionate, 10 mg. three times weekly, were then begun. After the fifth injection, he began having morning erections and occasional nocturnal emissions. After four weeks of treatment, increase in the size of the penis was noted and the scrotum was becoming the serrated, adult type. Consequently, the dosage was reduced to 10 mg. twice weekly. The penis continued to increase in size, and pubic hair became more abundant. He had then received a total of 330 mg. in three months, with continued improvement. The voice had deepened and the general body contour was more masculine. No facial or axillary hair had appeared as yet. Erections and ejaculations were of frequent occurrence. Treatment was interrupted at this point, and the patient was not seen again for fourteen weeks. The penis and testes were definitely smaller than at the previous visit, and he advised that erections ceased ten days after the last injection.

Case 5.—R. B., a white boy, aged 9, presented a typical Frohlich's syndrome. Both testes were descended, but the penis was quite small and underdeveloped. Roentgenograms of the wrists and sella showed nothing abnormal; the blood and urine were normal. The early stages of the treatment were directed toward combating the obesity. The usual measures were employed, and within three months the boy's weight was reduced sufficiently to bring him within the average weight limits for his age. Injections of anterior pituitary gonadotropic hormone, 400 units weekly, were given for a period of three months. No development of the penis occurred. Testosterone injections were begun in 10 mg. doses twice weekly. After the thirteenth injection, the penis was definitely growing and erections as frequent as three to four times weekly were reported. Treatment was stopped after the twenty-fifth injection. Four months later the penis had regressed somewhat and the erections had ceased. Treatment was resumed and continued without interruption for another four months. The phallus increased to normal, pubic hair became abundant, there were erections daily, but no ejaculations. During the past five months he has had no treatment, there has been very little decrease in size of the penis, erections continue with about the same frequency, but still no ejaculations. He is now 12½ years old, and normal osseous progress shown by the x-rays has been unaffected by the treatment.

Case 6.—R. N., aged 12 years, complained of overweight and enuresis. The patient presented a classical adiposogenitalism with mammary padding and abdominal folds. Both testes were descended, although underdeveloped. Findings of routine laboratory examinations were essentially normal. The treatment with testosterone propionate, 10 mg. two times weekly for thirteen weeks, promoted development of the genitalia. The penis increased in size and thickness and occasional erections and ejaculations were experienced. The testes showed no further growth. The enuresis decreased in frequency, and for a period of two weeks there was no bed wetting. At present, 5 mg. of the androgen are being given twice weekly. The enuresis is improved, although not entirely controlled. There are occasional erections and ejaculations, and the genitalia are showing continued development.

Case 7.—B.D.A. (*Fig. 1*), hypogonad, aged 42, had previously been diagnosed and treated elsewhere for hypothyroidism, without improvement. Injections of 25 mg. of testosterone propionate twice weekly were begun, and after six weeks there was marked sex urge and ability, and increasing hair growth over the pubes. The dosage was then increased to 25 mg. three times weekly and continued without interruption for four months. At the end of this period the facial and body hair had increased, sexual desires and ability were apparently normal. The prostate was of fairly normal contour, but very small and tender. At this time, injections were discontinued, and he was advised to apply 4 grams of the ointment, containing 8 mg. of testosterone, nightly on the abdomen. These topical applications have been continued during the past nine months, and he states that these are as effective as the injections. The penis has now developed to normal size and there is a scant amount of pubic hair, though the axillary hair has increased and he is now shaving every other day, whereas formerly he shaved only once every two weeks. He states that he indulges in satisfactory sexual intercourse two or three times per week.

Case 8.—B.A. (*Fig. 2*), aged 18, received twenty-four weekly injections of 75 mg. of testosterone propionate. After the injections were discontinued he was advised to rub in 2 grams of the ointment nightly. He returned four weeks later and reported that though he continued to have daily erections, ejaculations had ceased since he began the ointment. The dosage was increased to 4 grams nightly, and upon his return a month later he stated that there had been definite return and increase in the ejaculations, comparable to the effects of taking the medication by hypodermic.

CONCLUSIONS

Thirty-six patients with pre- or post-puberal hypogenitalism have been observed and treated over a period of ten months to three years with testosterone propionate by injection and by percutaneous administration. Eight of these considered typical of the group are reported in detail. In every instance there was an increase in the growth of the penis, incitation of libido and potentia coeundi, to the point where sexual intercourse could be performed satisfactorily. There were also an increased hair growth, deepening of the voice in many instances, and other signs of masculinity. The mental attitude of these patients changed remarkably. The major-

ity of them had a definite sense of inferiority which changed to an aggressive masculine type of behavior as treatment progressed. Ejaculations occurred in all adult patients, but no spermatozoa were found in the ejaculate. Testicular atrophy did not occur in any of the patients. No evidence of epiphyseal closure was noted, though frequent roentgenograms were made

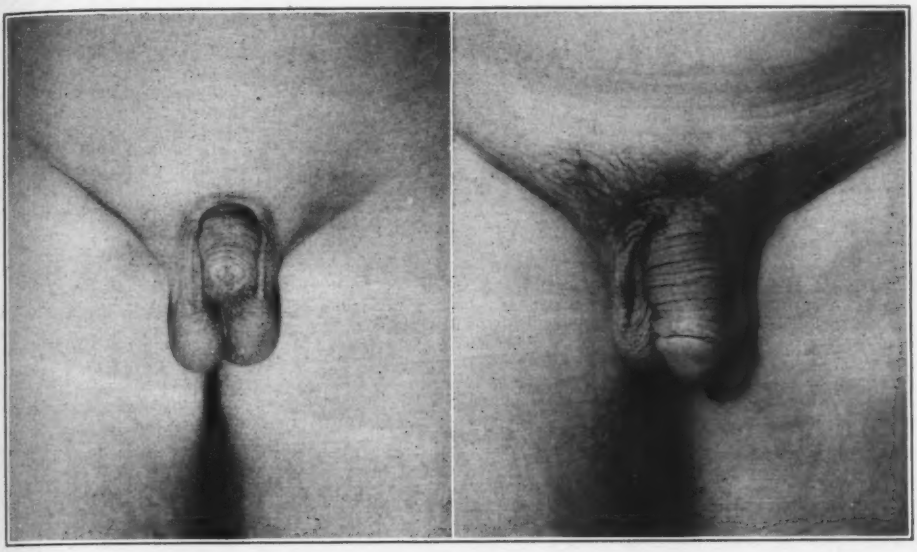

Fig. 1

Before and after treatment. Normal libido and potentia coeundi after injection of 25 mg. testosterone propionate three times weekly for sixteen weeks, and maintained by daily percutaneous administration of 8 mg.

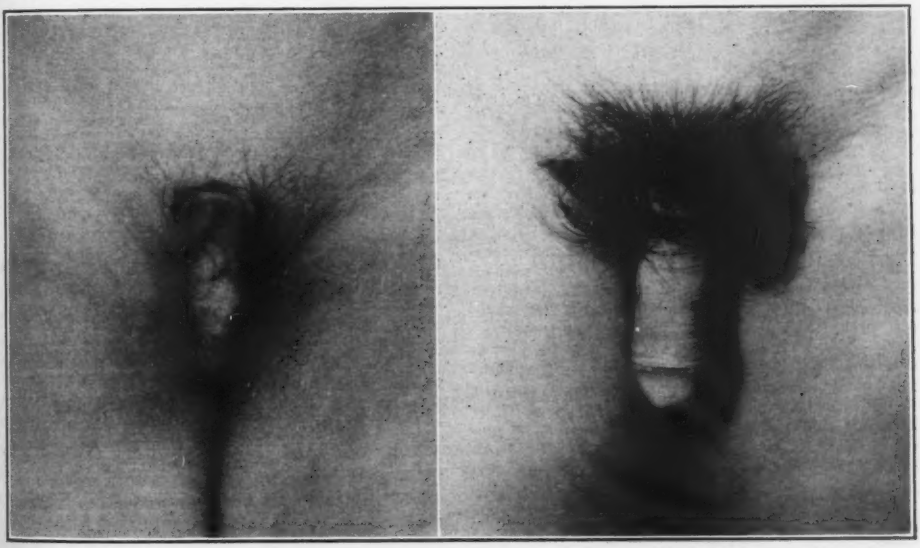

Fig. 2

Before and after twenty-four weekly injections of 75 mg. testosterone propionate.

throughout the period of observation. No untoward effects occurred. It is of interest to note that though in all patients discontinuance of treatment resulted in regression in the size of the penis and decrease of libido and erectile powers, this does not seem to be permanent in the prepuberal adioposogenital type in which adolescence appears to progress normally.

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DISCUSSION (*Abstract*)

Dr. Daniel L. Sexton, St. Louis, Mo.—Photographic evidence, as presented by Dr. Turner, is so convincing that I am sure there will be no disagreement as to the effectiveness of this hormone on genital growth.

It must be remembered that the essayist has limited his discussion to that group of individuals who showed a distinct lack of testicular stimulation. There has been a general agreement among those who have used this hormone as to the changes it produces, as outlined by Dr. Turner. Any variations from these must be considered as exceptions, and if there have been any unfavorable results, it has probably been due to an overdosage of the hormone.

It was stressed that in the prepuberal group there is no danger of epiphyseal closure and this, I agree, is the general rule. However, I have observed an instance in a boy 22 years of age in whom epiphyseal closure occurred after 3,100 mg. In Dr. Turner's series larger doses than this were employed without evidence of epiphyseal closure, so I feel that one need not fear arrested growth following the use of this hormone.

Priapism, that occurs with large dosages, is, of course, an unfavorable effect, particularly in the prepuberal group. This can be avoided by regulating the amount administered.

Probably the commonest question confronting this group is: what will this hormone do in the so-called male climacteric? It is generally agreed that when there is reduction in testicular function, this hormone will be effective, but when there is a general constitutional breakdown, disappointment will follow its use. No doubt, discouraging results can be expected when this hormone is used indiscriminately in men between 45 and 50 years of age, who number among their complaints a reduction in libido. Only a limited number have a testicular deficiency, and this group alone can expect benefit. The analogy to this state is the menopausal period in women. Certainly all of the complaints that occur at the menopausal period in women are not due to ovarian failure, and they certainly are not corrected by the follicular hormone. The indiscriminate use of testosterone propionate in the male should be condemned, and only when there is reasonable evidence of a reduction in testicular function may one expect benefit from its use.

It is also generally agreed that this hormone has no beneficial effect on spermatogenesis; in fact, large doses may serve to suppress sperm formation. I am heartily in accord with all that has been said about this hormone, and with the exception of priapism and occasional acne that follows its use, I know of no other unfavorable effects on any other systems of the body.

Dr. William J. Norfleet, Shreveport, La.—There is very little left for me to say on this subject, as Dr. Turner and Dr. Sexton have covered it very thoroughly. However, there are a few points that I should like to stress.

First, I hope that within the near future we shall have a more definite and complete, but simplified, laboratory technic which will enable us to determine the amount of the male hormone present in the body in order that a standard may be established to permit scientific administration of this hormone. Secondly, I trust that the profession will not permit the use of this particular substance to become as confused as the present status of the female sex hormone, as you undoubtedly realize that the laity quite often requests the female sex hormone when it is unnecessary because of high-powered salesmanship through the representative of many of the pharmaceutical houses.

I should like to ask Dr. Turner if he has had any experience with the effects of the male sex hormone on the peripheral vascular system. Personally, I have had none, but recently several reports have been published stating that this substance is beneficial in Buerger's disease where there is a definite disturbance of the peripheral circulation of the extremities.

There is a large group of cases which received beneficial effects from the administration of this drug. These are the benign hypertrophies of the prostate, and they are of particular interest to the urologist as well as to the internist. So far, it seems that by the administration of the male sex hormone temporary relief may be obtained and often there is a definite shrinking in the size of the prostate. Therefore, I believe that in the future the administration of this product will be one of the methods of treatment in early benign prostatic hypertrophies.

Among the large group of elderly males who complain of impotence, many times the administration of the sex hormone does not improve this condition. However, it does improve their general feeling and gives them a sense of well being.

Recently some authors have claimed some improvement in enlargements of the male breasts by the administration of the male sex hormone. I have had no experience with this and should appreciate some remarks by Dr. Turner on this subject in closing.

Dr. Neuton S. Stern, Memphis, Tenn.—Does testosterone cause cessation of overgrowth in height in the event the epiphyses do not close?

Dr. Hugh J. Morgan, Nashville, Tenn.—I should like to ask Dr. Turner to tell us about his methods of determining which pre-adolescent patients with hypogenitalism should receive specific treatment. It is a fact, I believe, that hypogenitalism in pre-adolescents very commonly spontaneously disappears and essentially normal maturation occurs with the lapse of time. Is it possible to select from the pre-pubescent children that he treats, and I am sure it is, I should just like him to enlarge upon it, those individuals who should be given the benefit of this drug in contradistinction to those who will without any treatment eventually mature?

The second point that I should like him to enlarge upon when he closes the discussion is whether or not

he has observed individuals, these young ones particularly, because they are the ones I am interested in, who have developed precocious sexuality or behavior changes as a result of treatment. Have they become promiscuous? Is it possible that specific treatment may make the adjustments of puberty, the problems of maturation, perhaps a little more vivid, a little more difficult? These are points to which I am sure Dr. Turner has given thought, and I raise these questions with the hope that he will enlarge upon them when he closes the discussion.

Dr. Turner (closing).—Genital development is about as variable as osseous growth. Some children develop earlier and some later than the average. It is true that some of these so-called prepuberal genital hypoplastics may mature normally. However, in a certain number of them the lack of sexual development is so marked that the need for treatment is obvious. In others this retardation results in inferior behavior mechanisms, to the point where they refuse to go in swimming in the nude, or enter into athletics or any activity which necessitates exposure in the presence of other boys. It is these youngsters in whom treatment is definitely indicated. It is gratifying, indeed, to observe their change to a normal personality as treatment progresses. Certainly, this hormone should not be given in sufficient amounts to produce precocious sexual maturity. The dosage can and should be gauged to bring the development up to only normal for the age.

In response to Dr. Stern: in all of my patients roentgenograms were made at frequent intervals and no evidence of osseous advancement or epiphyseal closure was noted.

Dr. Norfleet very properly remarked on some of the advertising of this preparation. Contrary to some manufacturers' propaganda, Ponce de Leon's secret has not as yet been discovered. I have purposely left out of my paper discussion of such conditions as prostatic hypertrophy and the effect of testosterone on the vascular system, except to say that blood pressure readings were taken in all of our adult cases and there were no changes whatsoever. The question has been raised as to the possibility of cerebral accidents in older men who are overstimulated by these preparations and who may get the idea that they are again in their second decade, but I think that danger is rather remote. A number of cases have been reported in only one article, to my recollection, on the use of this substance in the treatment of peripheral vascular disease. I have not used it in this condition, but there is a possibility, of course, of benefit from the general increase in tonicity of the vessels.

I have some slides of gynecomastia that I did not show. We have had no success in reduction of the breasts where there was normal genital development. Gynecomastia occurring in youngsters who have not matured, in the hypogenital types, and in castrates can frequently be reduced by the injection of testosterone.

Dr. Morgan.—Tell us what are the behavior problems in the pre-adolescents as the result of treatment. I think that is important.

Dr. Turner.—I have observed no untoward effects on behavior. Its use in prepuberal boys, as stated previously, should be restricted to those with definite genital infantilism and to prevent or correct the psychic trauma frequently associated with this condition. It should also be reserved only for those who have not responded to injections of anterior pituitary or anterior pituitary-like gonadotropins. Some degree of caution and common sense must be used in the prescription of this substance.

CHOICE OF HORMONE TREATMENT IN MALE SUBGENITAL DEVELOPMENT*

By DANIEL L. SEXTON, M.D.
St. Louis, Missouri

Surgical treatment of cryptorchism is not without disappointment, as shown by the report of Burdick and Coley,[1] who found in an analysis of 537 orchidopexies that intrascrotal placement occurred in 50 per cent, with subsequent growth and development satisfactory in but 15 per cent. It must be admitted that these results might be different in the hands of surgeons who are doing a great deal of this work, but since the treatment of patients is widely disseminated, these results probably bespeak the average. On the other hand, hormone therapy has been credited with overcoming cryptorchism in 50 per cent of the cases treated and with enhancing the chances for a good surgical result when this procedure is indicated.[2]

Three forms of hormone treatment are available, namely: pituitary gonadotropic hormone, anterior pituitary-like hormone, derived from placenta, and the male sex hormone (testosterone propionate). Following the isolation of the gonadotropic hormone almost simultaneously by Aschheim and Zondek[3] and Smith and Engle,[4] experimental results showed this hormone to be an effective sex stimulator. Clinical reports have not been encouraging, however, and this hormone has been employed sparingly. This is not true of the anterior pituitary-like hormone, which is widely used and is considered the hormone of choice. Testosterone propionate has very little effect on the testes, but does have a most decided effect on other genital structures and on the development of masculine traits.

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*Read in Section on Pediatrics, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*From the Department of Medicine, St. Louis University, and the Endocrine Clinic, Firmin Desloge Hospital.

*Acknowledgment is made to Dr. E. A. Sharp, Parke, Davis & Company, for a generous supply of "antuitrin-S" and to Dr. Max Gilbert, Schering Corporation, and Mr. R. C. Mautner, Ciba Company, who furnished testosterone propionate for these studies.

PITUITARY GONADOTROPIC HORMONE

The effectiveness of this extract of the anterior hypophysis of animals has been proven beyond doubt experimentally. Its clinical use by the writer has been limited to three cases of cryptorchism, one of which was bilateral, and to a case of retarded genital development. In all instances it had little effect. The case of bilateral cryptorchism received 5,400 rat units without appreciable benefit and subsequently, following the administration of anterior pituitary-like hormone, the right testicle descended after 3,600 rat units, and descent occurred on the left side after a total of 31,000 rat units of the latter hormone.

ANTERIOR PITUITARY-LIKE HORMONE

Reports on the use of this hormone have been numerous. Turner[5] summarized 320 cases of cryptorchism by 23 authors in which descent was reported in 60 per cent. Zelson,[6] in another summary, reported cryptorchism overcome in 51 per cent. Individual reports, with considerable variance in results, include those of Thompson and Heckel,[7] who had favorable results in but 17 per cent of 60 instances. Wilson,[8] who obtained good results in 30 per cent of 17 cases, and Dorff,[9] who reported descent following rather large doses in 9 of 12 patients.

Some writers[10 11 12] are of the opinion that this hormone merely hastens descent and that it will not overcome cryptorchism that would not otherwise have been corrected spontaneously. There is no basis for denial of this statement, but on the other hand, there is no proof of its accuracy, for the fact remains that many men go through life with cryptorchism. Assuming that delayed descent and development were the only harmful effects from watchful waiting, these factors alone would justify active therapeutic measures, for most boys with imperfect testicles show characteristic traits, even in the prepuberal age.

There has been considerable discussion as to the age when hormone treatment should be instituted. Cabot[13] advocates starting hormone therapy between the ages of 3 and 7. Nixon's[14] series included boys from 2½ years up, and other pleas for early treatment come from Zelson[6] and Rubenstein.[15] The latter urges early treatment to avoid skeletal disproportion and persistent hypoplasia and the all-important problem of psychic difficulties. Mimpriss[16] suggests starting treatment at the age of 10, reserving it for those in whom spontaneous descent seems unlikely. It is generally agreed that results are much better at puberty, when adolescent awakening is at its height, but oftentimes the boy's psychic and physical make-up suffers if treatment is delayed until this period. Undoubtedly, the time to start treatment must be individualized, and no set time can be given without reservation. The author feels that even the less severe cases of cryptorchism should be treated not later than 10 years of age, while treatment for the more severe ones should be instituted at about 6. Rarely will there be need for starting earlier. Subgenital development without cryptorchism may be treated with good results up to any time through adolescence.

A question of importance is dosage. Bigler,[17] *et al.*, believe encouragement follows 4,000 rat units, if descent is to occur. Wilson[8] used 10,000 rat units in ten weeks to obtain 30 per cent descent. Zelson[6] states that successful results should be expected after 10,000 units. The writer,[18] in a previous communication, stated that after 5,000 units results may be expected, and at this writing he feels that with rare exception, 5,000 rat units, over a period of 10 to 15 weeks, and certainly a total of 10,000 rat units over 20 weeks, will promote descent, if it is to occur. Large, continuous doses had better be avoided, as shown by Thompson and Heckel,[19] and if treatment is to be prolonged, rest periods of three months are advisable.

In addition to the specific effect of anterior pituitary-like hormone on testicular development, this hormone has a general maturing effect on the entire organism, which is undoubtedly due to the increased interstitial growth of the testes. The maturity effects include psychic development when lagging, a desire for increased activity where lethargy has prevailed, not infrequently a redistribution of weight; and finally a tendency to overcome effeminate traits. Schaefer,[20] *et al.*, have well summed up the effect of this hormone by terming it the maturing factor of the gonads.

Anterior pituitary-like hormone may be used effectively in those cases of cryptorchism with hernia, where surgical interference is obvious. Not infrequently, the testicle can be increased in size, thereby enhancing the chance for a good operative result. Following orchidopexy, in which the testes are small, treatment again may be used effectively in increasing testicular size, thereby aiding in the fixation of the testis in the scrotum.

In *Table 1* are shown 45 instances of cryptorchism in 33 boys, ranging in age from 3 to 15 years. Cryptorchism was bilateral in 12 instances, present on the left side in 12 and on the right in 9. Total descents numbered 21, or 47 per cent. Of the total 21 instances of descent, 10 occurred on the right side and 11 on the left. Of the 12 bilateral cases, both testes descended in 3. In the last 22 instances of cryptorchism in 16 boys, descent has occurred in but 6, or 27 per cent.

The smallest dose required (*Case 1*) was 1,000 rat units in a boy 3 years of age with left cryptorchism. Treatment in this boy had been immediately preceded by the injection of 150 mg. of male sex hormone, which had been given without effect on testicular site. The largest amount used, 60,000 units, was in a boy 11 years of age with bilateral cryptorchism, who previously had had an unsuccessful right orchidopexy (*Case 23*). Before starting treatment on this boy, neither testicle could be defined and at the termination of the treatment a small left testicle was at the external ring on the left side. Eleven of 33 boys treated received dosages larger than 10,000 units for the reason that descent had not occurred on this amount. With the exception of *Cases 28* and *30*, larger doses were no more effective than the smaller ones, and there is no proof, especially in *Case 28*, that a smaller dose would not have been as effective had there been an intervening rest period.

Table 1

RESUME OF CASES TREATED WITH ANTERIOR PITUITARY-LIKE HORMONE

Case	Age	General Type	Position of Testes				Total Treatment Rat Units	Comments
			Left		Right			
			Before	After	Before	After		
1	3	obese	O	S	S	S	1,000	150 mg. M.S.H. before APL
2	4	normal	C	S	S	S	2,400	
3	5	frail	C	S	S	S	8,600	
4	5	normal	C	S	S	S	3,200	
5	5	frail	C	C	S	S	8,200	
6	5	frail	O	O	ER	S	18,000	Hypospadias
7	6	frail	O	O	O	C	8,400	Rt. side previously operated unsuccessfully
8	6	frail	S	S	O	S	2,000	430 mg. M.S.H. before APL
9	6	frail	O	O	S	S	10,500	465 mg. M.S.H. before APL
10	7	normal	O	O	O	O	3,400	
11	8	frail	O	O	O	ER	27,000	Subsequent successful operation
12	8	normal	O	O	S	S	4,200	
13	9	obese	O	O	C	S	2,000	
14	9	frail	S	S	O	O	26.000	
15	9	obese	C	C	C	C	10,005	
16	10	obese	O	ER	C?	S	4,800	
17	10	obese	SP	S	S	S	7,000	
18	10	obese	C	S	S	S	8,400	
19	10	obese	S	S	O	O	28,000	
20	11	normal	S	S	O	S	7,000	
21	11	frail	S	S	ER	S	1,800	
22	11	frail	S	S	ER	S	1,700	
23	11	obese	O	ER	O	O	60,000	Previous unsuccessful right orchidopexy
24	11	obese	O	O	S	S	43,000	Left cryptorchism persists after 37,000 rat units
25	11½	frail	S	S	O	ER	11,600	
26	12	frail	ER	S	ER	S	8,900	
27	12	obese	O	S	C	S	3,300	
28	12½	frail	O	S	O	S	31,200	
29	13	obese	S	S	O	O	5,900	
30	13½	obese	S	S	ER	S	16,800	
31	15	normal	C	ER	S	S	7,800	
32	15	thin	O	O	O	ER	15,000	Previous unsuccessful bilateral orchidopexy
33	15	normal	C	S	S	S	8,400	

C—canal. S—scrotum. O—undefinable. ER—external ring. SP—suprapubic.

It was formerly thought that the obese type would be more likely to respond than the normal or frail types and in this series this same thought holds. Redistribution of weight occurred in 6 of 12 boys, loss of weight being noted particularly over the mons, breast and girdle areas. This improvement is considered secondary to increased testicular function. Thus, it would seem advisable to add anterior pituitary-like hormone to other indicated measures in the management of adiposogenitalism in the male.

A point that has focused the attention of the writer is the failure to descend, in four instances, of well-developed testes in the canal. Three of these four were operated upon after hormone treatment had failed, and adhesions were found which would have made it impossible for descent to occur. The writer is of the belief that hormone therapy is useless in undescended testes that are well developed.

No side effects from this hormone have been observed when the dosage was controlled. Prolonged large doses will produce precocious development, which is certainly an undesirable effect. While spermatogenesis is not a problem in the preadolescent boy, yet it is important to know that this hormone has no depressing effect on sperm formation; on the other hand, the evidence points in the other direction, that of producing spermatogenesis.[21-23]

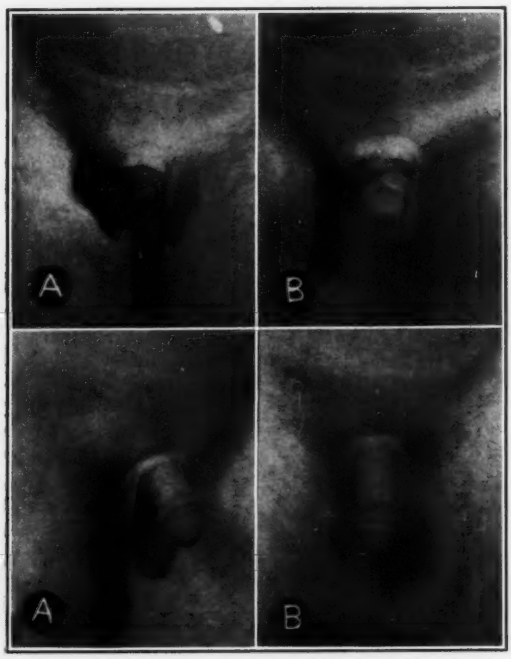

Fig. 1

A (top). Age 10. Testes descended but small. B (top). After 6,000 rat units anterior pituitary-like hormone over ten weeks. A (bottom). Age 13½. Right testicle at external ring. (*Case 30, Table 1*). B (bottom). Twenty weeks after 16,800 rat units anterior pituitary-like hormone.

SYNTHETIC MALE SEX HORMONE: TESTOSTERONE PROPIONATE

Experimental and clinical reports[24-28] indicate that testosterone propionate is the most potent male sex hormone available. Following the use of this hormone in the prepuberal age, writers are in accord that it causes growth of the penis, priapism, pubic and body hair growth, enlargement of the larynx with deepening of the voice, frequently facial acne, increased body weight, nocturnal emissions and psychic stability. In addition, Hamilton and Huber[29] reported the successful treatment of cryptorchism in boys ranging in age from 1½ to 17 years, obtaining descent in 9 of 25 instances (36 per cent). In an additional 12 cases of pseudocryptorchism they reported that small amounts conditioned the testes against spastic retraction.

It was because of this report that 18 boys from 3 to 15 years of age with subgenital development, 9 of whom had cryptorchism, were treated with testosterone propionate. It was hoped that this hormone would replace or enhance the effect of anterior pituitary-like hormone in the treatment of cryptorchism. Results, however, have been disappointing as shown in *Table 2*.

In one instance, *Case 12, Table 2*, the left testicle, which had previously been in the canal, descended into the scrotum, but retracted. In this same boy spastic retraction, which had been present on the right side, subsided after treatment. In a second instance (*Case 14*) spastic retraction on the left was overcome. Aside from these two instances, no effect on cryptorchism was noted in the 12 instances present in 9 boys, nor was there any significant effect on the size of the testes in the scrotum in any of the other boys. However, this hormone had a very decided effect on penile growth, production of priapism, pubic hair growth and weight increase. Maturing psychic and increased masculine traits were noted in most instances. None of these prepuberal boys

Table 2

RESUME OF CASES TREATED WITH SYNTHETIC MALE SEX HORMONE

Case No.	Age	Treatment			Position of Testes			Size of Testes[1]		Penile Growth	Priapism	Pubic Hair Growth	Nocturnal Emissions	Maturing Effect	Weight Increase	
		Mg.			Left		Right								Pounds	
		Weekly	Total	Duration Weeks	Before	After	Before	After	Before	After						Actual	Anticipated[2]
1	3	5	65	13	S	S	S	S	2+	2+	0	0	0	0	0	2½	1
2	3	20	150	8	S[3]	S[3]	0	0	3+	3+	2.3 cm.	yes	1+	0	0	4	2/3
3	5	10	80	8	S[3]	0	0	0			3.0 cm.	0	0	0	slight		¾
4	6	50	430	9	S	S	0	0	1–2+	1–2+	2.9 cm.	yes	1+	0	yes	7½	1
5	6	50	465	10	0	0	S	S	1–2+	1–2+	1.5 cm.	yes	1+	0	yes	0	1
6	7	20	180	9	S	S	S	S	4+	4+	0.5 cm.	0	1+	0	0	11½	1
7	7	50	375	8	S[3]	S	S	S	2+	2+	2.0 cm.	yes	1+	0	yes	9	1
8	10	20	600	30	S	S	S	S	2+	3+	2.8 cm.	0	4+	0	yes	18	4
9	10	20	460	23	S	S	S	S	2+	2+		0	1+	0	0	14	4
10	10	20–30	140	7	S	S	S	S	2+	2+		0	0	0	0	2	½
11	10	50–75	475	8	S	S	C	C	3+	3+	1.5 cm.	yes	2+	0	yes	6½	1½
12	11	50	760	14	C	S	S	S	2+	2–3+	2.0 cm.	yes	3+	0	slight	14	1
13[4]	11	100	900	11	0	0	0	0			3.3 cm.	yes	3+	0	yes	10	1½
14	12	50–75	1125	20	S[3]	S	S[3]	S[3]	2+	3+	1.8 cm.	yes	3+	0	yes	14	3
15	12	50	625	12	0	0	S	S	4+	4+	2.0 cm.	yes	2+	0	slight		1½
16	13	10	360	36	S	S	S	S	2+	3+	2.8 cm.	0	3+	0	yes	11	4½
17	13	10	120	12	S	S	S	S	4+	4+		0	2+	0	0	6	1½
18[5]	15	50	450	10	0	0	0				2.3 cm.	yes	4+	0	yes	6	2

1. Refers to testes in scrotum.
2. From "Endocrine Medicine," Englebach. Charles C. Thomas Co., Springfield, Illinois.
3. Spastic retraction of testicle.
4. Had 60,000 r. u. APL before M.S.H.
5. Had 15,000 r. u. APL before M.S.H.

C—canal. S—scrotum. O—undefinable.

had nocturnal emissions which have been observed in older boys.

It is agreed that precocious penile growth, priapism and pubic hair growth are most undesirable in young boys, and since these unfavorable effects do occur and there is practically

Fig. 2

A. Age 6. Left cryptorchism. (*Case 5, Table 2.*) B. After 465 mg. testosterone propionate over ten weeks. Cryptorchism unchanged. Penile growth of 1.5 cm. Note general improvement.

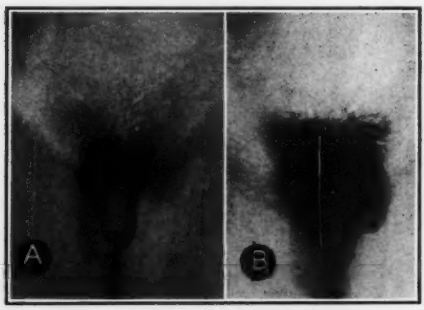

Fig. 3

A. Age 15. Unsuccessful bilateral orchidopexy. (*Case 18, Table 2.*) B. After 450 mg. testosterone propionate. Testes unaffected.

no effect on testicular development, this hormone is not advocated for the treatment of cryptorchism or where increased testicular development is the objective. However, the male sex hormone does occupy a place in the management of certain types of subgenital development in prepuberal boys. In frail boys where subgenital development is part of the general constitutional deficiency, increased weight and general constitutional improvement may be anticipated. The dosage, however, should be limited to 5 to 10 mg., one to two times weekly, or to that amount which will not produce undesirable precocious sexual changes. In those instances of cryptorchism where anterior pituitary-like hormone and surgical treatment have failed and eunuchoid characteristics prevail, the male sex hormone in doses of 25 to 50 mg. weekly for 10 to 20 weeks will bring about development of the penis, pubic hair growth, deepening of the voice, psychic stability and control, improved physical stamina and increased confidence, which is woefully lacking in an eunuchoid boy. The hormone is substitutional and after the desired effects are obtained, a maintenance dosage must be continued. This may be accomplished either by inunction, by subcutaneous pellet implantation, or by weekly or bimonthly intramuscular injections. The hormone may be of help primarily in operations for hypospadia such as outlined in *Case 3, Table 2.*

While testosterone propionate is not advocated in malnutrition, attention is called to *Cases 6* and *17, Table 2.* In *Case 6* all of the accepted measures for increasing weight had failed, yet after 9 weeks' treatment with a total dosage of 180 mg. of male sex hormone, this boy's weight was increased 11½ pounds.

CONCLUSIONS

Pituitary gonadotropic hormone is relatively ineffective in the treatment of cryptorchism and subgenital development. Combined with anterior pituitary-like hormone, it may have a decided beneficial effect through its synergistic action. So far no clinical reports substantiate this thought.

Anterior pituitary-like hormone is the choice of available hormones in the treatment of cryptorchism and underdeveloped intrascrotal testes. From conservative reports, descent may be anticipated in 25 to 35 per cent of all cases treated. With rare exception the dosage will not have to exceed a total of 10,000 rat units administered over a period of 16 to 20 weeks. Again it is

with exception that treatment should be started before the age of 6 and preferably not after the age of 10. The only side effect to be avoided is precocious genital development which follows prolonged large doses, especially in the young. This hormone without any other treatment will bring about a redistribution of weight in about half of the obese boys through the medium of increased testicular function. It should be added to the therapeutic program in male adiposogenitalism. It may be used preliminary to orchidopexy to enlarge the testicle and scrotum and thereby enhance the chances for a good surgical result. As a postoperative measure, it may be used effectively to help fix the testes in the scrotum.

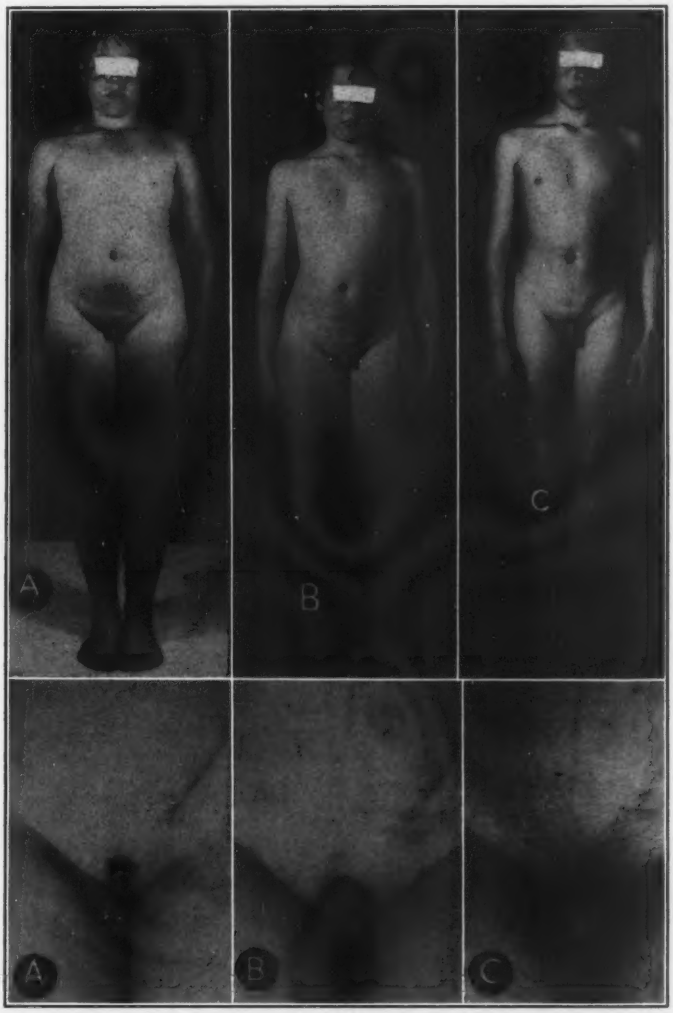

Fig. 4

A-A. Age 11. Bilateral cryptorchism. After unsuccessful right orchidopexy. (*Case 13, Table 2.*) B-B. Sixteen months later, after 60,000 rat units anterior pituitary-like hormone. Small left testicle in lower canal. C-C. Twenty-two months later, after 900 mg. testosterone propionate. Penile growth of 3.3 cm. Testes unaffected. Sparse pubic hair. Note maturing effect.

The use of the male sex hormone is limited to those cases of marked hypogonadism which have failed to respond to the anterior pituitary-like hormone or to surgical interference. Testosterone propionate has no appreciable effect on testicular development or on cryptorchism. It has a remarkable effect on penile growth, pubic hair growth, and the development of masculine traits. It will oftentimes bring about an increase in body weight in cases of malnutrition where all other measures have failed. It has a most decided effect on psychic maturity and on physical inertia. Occasionally facial acne may follow its use. In the group studied there was no evidence of hastened epiphyseal closure. The unfavorable side effects are priapism and precocious penile growth, which may be avoided by controlled dosage. The hormone is substitutional and must be continued with maintenance dosages which are individual.

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DISCUSSION (*Abstract*)

Dr. Henry H. Turner, Oklahoma City, Okla.—I find myself completely in accord with Dr. Sexton's conclusions, with the exception, perhaps, of his statement regarding anterior pituitary gonadotropic fractions, but inasmuch as he said he felt they were relatively ineffective, our differences are probably more apparent than real. Although recognizing the fact that these cases of adiposogenitalism are probably more of a neurohypothalamic origin than pituitary, I feel that the anterior pituitary gonadotropic hormone is probably indicated and that it is probably more effective when combined with the pregnancy urine hormone of which he spoke. I do believe there is a synergism between the two and that better results will be obtained if they are combined.

I reported a series of some 26 cryptorchids before the meeting of this Association in New Orleans two years ago. My conclusions at that time reported successful descent in 53 per cent of these patients using anterior pituitary gonadotropic and anterior pituitary-like fractions. We had partial descent in 30 per cent and failure in 15 per cent, which I believe today was due to inadequate dosage. We are now giving a much higher unit of dosage; it is not unusual to give 2,000 to 3,000 units of APL a week to these patients.

I am definitely of the opinion that hormonal therapy should be tried in every cryptorchid patient, preferably, perhaps, before the eighth year. I am not unmindful of the fact that many of these non-descended testes may come down spontaneously even in the twelfth or thirteenth year, but, as Dr. Sexton has pointed out, the scrotum is the normal habitat of the testes, and the quicker we get them where they belong, the more likelihood of a functioning organ. It has been shown experimentally that retention of the testis in the abdomen interferes with its development; therefore, if the scrotum is the normal place for the testes, why not attempt to locate them there as soon as possible?

I have been considerably interested in testosterone propionate, and about a year ago reported 54 patients whom we had treated with this hormone, including cases of hypogenitalism and other genital anomalies and dysfunctions. I am presenting a further report on this subject before the Section on Medicine Friday morning. Here again, I find myself in complete accord with Dr. Sexton as to the treatment of subgenitalism. Certainly, testosterone does promote both primary and secondary sex characters, and its effect on the general health of men in their senescence is quite remarkable.

We have treated some 80 patients with testosterone, and in no instance to date has there been any evidence of testicular atrophy. I have repeated x-rays of my patients and have noticed no evidence of osseous advancement or epiphyseal closure. If testosterone is given in therapeutic doses, I do not believe that testicular atrophy or epiphyseal closure will result. Dr. Sexton has demonstrated three very potent substances here this afternoon, and a certain degree of caution must be used in their administration.

Dr. Luther W. Holloway, Jacksonville, Fla.—I am an endocrinologic neophyte and I feel very much out of place in this vast company in discussing some of these nebulous things. I have the conservative attitude of a country pediatrician, that these substances recommended should be used with great caution and not in a widespread manner until the proper indications are clearly defined.

My confreres and I in Jacksonville observed about 21 cases of different subgenital developments, mostly cryptorchidism. We let nature take its course in most of them and I think 20 of them did their stuff unaided by endocrine glands, and one came to surgery. From the reports, they are all functioning now as normal male beings should.

The incidence of underdevelopment is rather low, and in big centers where facilities exist for the careful determination of the facts they can be studied much better than we can study them out on the frontiers of the knowledge of medical endocrinology, and of course very few of us have the set-up to do the monumental work that Dr. Talbot has done in Boston, or Dr. Sexton has done in St. Louis. The gist of my discussion is to be conservative, for old nature usually does a good job.

Dr. Fritz B. Talbot, Boston, Mass.—I have been very much interested in Dr. Sexton's paper because, although I disagree with some of the conclusions, it is a record of very interesting physiologic reactions.

The percentage of cryptorchids among drafted soldiers was very low indeed, and the percentage of cryptorchids in children is considerably higher. We must explain the discrepancy in incidence, and I see only one explanation, and that is that cryptorchids tend to become normal without medication.

In the second place, we want to be sure that we are dealing with a cryptorchid. It is customary to have the patient lie for one hour with heat applied over the inguinal region. It is found that in a large number of instances the testes come down.

I cannot agree with all that Dr. Sexton said about the treatment of obesity. There is plenty of evidence in the literature that fat children with big breasts, excessive fat around the pelvic girdle, and seemingly small genitalia will straighten themselves out when the diet is reduced sufficiently. I will admit that small doses of thyroid can be given without causing the symptoms that I describe, but I do not think that thyroid is indicated unless the metabolism is lowered. I do not admit that the metabolism of these children is low when standards which take into consideration the composition of the body are used. I mean by that the standards of total calories for the height and the total calories for the weight.

In the physiologic activity of testosterone, a very complicated action takes place. It has been established that testosterone depresses the luteinizing hormone of the pituitary, which is necessary for the secretion of testosterone, and you can see that if we supply testosterone there is the theoretical danger of atrophy of the male interstitial cells, whereas the pregnancy urine gonadotropic hormone stimulates the interstitial cells and as a result stimulates secretion of testosterone.

I see around here plenty of men of my own generation who have seen many new therapeutic agents come and go. Since there is physiologic evidence that testosterone can cause atrophy of the testicles of rats, we have to be suspicious of its action in the human being. It is known to suppress the formation of spermatozoa in young adults.

You can have the eunuchism of the Turks and you can have physiologic eunuchism, from old age or other causes, or injury. You can even have eunuchism in children. If these very active substances are used the urinary hormones should be measured, so that you will know what you are doing. The male sex hormones can be measured today.

Dr. Sexton (closing).—Dr. Turner and I have differed as to the effect of the pituitary gonadotropic hormone before, and I see that we are not together yet.

He has stressed the fact that the use of testosterone propionate over a prolonged period has shown no effect on epiphyseal closure. I have noted an exception to this rule in a boy 22 years of age.

Dr. Holloway has approached the subject with a conservative attitude which I can well appreciate. It is agreed that many preadolescent cryptorchids have spontaneous descent at adolescence. However, it is my belief that a large majority would descend late and in the meantime the boy would suffer the effects of delayed or diminished testicular stimulation. Furthermore, it must be admitted that cryptorchidism is encountered in adult life, a condition that might have been prevented by proper medical attention.

In reference to Dr. Talbot's discussion, it was not my intention to convey the idea that every fat boy should have treatment with one or more of the hormones. When I am confronted with a problem of juvenile obesity, I want to size up the parents, for many of these boys are of a family type and are normal in every respect except that they have congenital obesity. I also want to learn all I can about the boy's personal habits, his physical activities, his attitude toward other boys and toward boys' games. These are facts of great importance in the history, and when I encounter an obese boy, who is mentally and physically lethargic, I have no hesitancy in prescribing thyroid for him, regardless of his basal metabolic rate. Of course, he is kept under careful observation until his tolerance or intolerance to thyroid is determined, and in every case treatment is individualized. I think one can assume a too conservative attitude on this subject, which often proves detrimental to the boy's progress. Experience has shown that endocrine therapy has done a great deal for certain types of juvenile obesity, not particularly from the standpoint of reducing weight, but in bringing about constitutional improvement.

As to diagnosis, all of these cases have had very careful study before being classified as cryptorchids. Cases of spastic retraction are common, probably more so than those of cryptorchism.

Prolonged treatment with large doses of testosterone propionate should be guarded against and maintenance dosages should be held to the minimum. This same principle should apply to the administration of pregnancy urine extract, and when there has been no evidence of testicular descent after 10,000 rat units of this hormone, a rest period should be given and only occasionally a subsequent second course administered.

TREATMENT OF FUNCTIONAL DISORDERS OF THE FEMALE BY RADIATION OF THE PITUITARY GLAND*

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and
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Irradiation of the pituitary gland and the ovaries has been before the medical profession since 1922 as a possible method of therapy of functional gynecological conditions. This method has not been widely adopted because the questions of its effectiveness, its mode of action and its harmlessness have never been satisfactorily answered.

As to its mode of action we can say no more today than we did in our original report[1] four years ago: that we do not know, but that the end results seem to be those of stimulation. We can say that it is safe. This is demonstrated by the fact that no damage occurs even with the large doses of irradiation used in treating tumors of the pituitary.

We recently irradiated the pituitary region of a series of rabbits with doses which, compared to those used in the human, would be excessive. We found no histologic evidence of primary damage to the pituitary or secondary degenerative changes in the ovaries, thyroid or adrenals. Others have reported similar findings.[2 3]

The reports in the literature on the use of irradiation[4-9] in the human have been few as compared to the large number of reports on the use of glandular preparations for such conditions. In such reports as have appeared, there is no complete unanimity of opinion. This is apparently due to differences in selection of cases, interpretation of results and technic used.

We have used irradiation of the pituitary gland in cases of functional disorders of women since 1930. Irradiation of the pelvis was reserved for only a few special cases. This report is concerned with the 243 cases in which we have been able to follow the cases over a sufficient period of time to evaluate correctly the results of therapy. Only patients who are still under our personal observation or who responded to recent questionnaires are included. The minimum time which has elapsed since therapy was 6 months, the maximum 9 years, the average being 2 years.

The irradiation therapy has been given by two groups of radiologists with a slight variation in technic. One used 200 kv., 25 ma., 50 cm. distance, filter 1 mm. al. and Thoreus equivalent to 2 mm. copper for 6 minutes, delivering 102 r, one treatment being given on alternate sides weekly for 3 to 4 weeks. The second method was 200 kv., 25 ma., 60 cm. distance, 0.5 mm. aluminum filters, delivering 130 r, one treatment being given every three weeks for 3 to 4 treatments. We have noted no appreciable difference between the two technics.

In the series of cases presented, all were private patients. The majority were also given some form of organotherapy. Irradiation was used in an effort to obtain the best results as quickly as possible and not as controlled experiments in the evaluation of irradiation. However, we feel that the examination of such a number of cases which have been followed over a sufficient period of time and in which endocrine therapy has been a constant factor should throw some light on the effectiveness of this mode of therapy. Particularly is this true when it is considered that the majority of these cases were treated when organotherapeutic agents were not nearly so potent as those which we have today. For instance, estrogenic substance in the early days was supplied in 50 units per c. c., gonadotropic in 10 to 100 rat units per c. c. Progesterone was not available for quite a while and then in one-twenty-fifth to one-fifth rat units. Today we have estrogenic substances in 50,000 units, gonadotropic substances much better standardized, more potent and with the addition of the new type derived from pregnant mare serum. Progesterone is available in 5 rabbit units.

In all cases, organic pelvic disease and systemic disease were ruled out as far as possible before therapy was begun. The cases are classified as to the chief complaint and response to treatment. Only those whose symptoms have been completely absent over the period of observation or up to the time of response to the questionnaires have been considered as "relieved." Those considered "improved" include also cases in which there was complete relief for a time with reversion later, but never to the original state. The "failures" are those in which there was no response to treatment or only tem-

*Read in Section on Radiology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

porary response with complete reversion to the original condition. The cases so studied may be classified as follows:

Chart 1
CLASSIFICATION OF CASES

Amenorrhea	27
Oligomenorrhea	39
Hypomenorrhea	21
Oligomenorrhea and hypomenorrhea	14
Polymenorrhea	41
Menopause	21
Dysmenorrhea, normal cycle	31
Sterility, normal cycle	20
Obesity, normal cycle	9
Miscellaneous, normal cycle	20
Total	242

DISTURBANCE OF MENSTRUATION

The correction of menstrual disturbances depends upon our ability to stimulate the ovary to normal function. This stimulation normally comes from the pituitary gland. In most instances of ovarian failure, with the resulting menstrual disorders, the fault is not primarily in the ovaries, but is secondary to pituitary failure. The different menstrual disturbances all represent faulty ovarian function which is nonspecific in type, but represents differences in degree of ovarian function. Irradiation of the pituitary gland is an attempt to stimulate the pituitary which would in turn stimulate the ovary. This type of therapy for ovarian failure is entirely logical since it is directed toward the etiology of the ovarian failure, namely, the pituitary failure.

AMENORRHEA

Chart 2
AMENORRHEA, 27 CASES

	Relieved	Improved	Failures
Number of cases	6	9	12
Average age	19	20	23
Endocrine stigmata	1	3	10
Subsequent pregnancies	2	0	1
Average time observed, yrs.	3	2	1½

There were 27 cases in which menstruation had failed to occur for at least four months. Twenty-three were secondary in type and 4 were primary. All cases received irradiation to the pituitary. In only one case was the pelvis also irradiated. A normal menstrual function was reestablished in 6 cases, periods occurred but not regularly in 9 cases, and in 12 no permanent results were obtained. In the last group 8 bled one to three times or had several periods of spotting, but because there was no semblance of regularity we considered them as failures. One of the failures had previously a partial resection of the ovaries and later developed symptoms of menopause. One case conceived during a period of amenorrhea, but her periods were not re-established after delivery.

Amenorrhea may represent profound ovarian failure to such a degree that the ovaries are not functioning at all and the uterus becomes atrophic, but it may also represent a fair degree of ovarian function in which the blood and urine levels of estrogenic substance are high and the uterus maintains its normal size. A case in point is that of a young girl who had not menstruated in 2 years, whose urine level of estrogenic substance was equal to that usually found in normal women premenstrually. She menstruated after only one x-ray treatment and has continued normally for one year since. She had been taking thyroid for over two years and the only form of therapy she received was irradiation. She evidently needed only a slight stimulation to change her function from a high subthreshold level to that of normal. This difference in degree explains the wide range of response to treatment.

The age and duration of the amenorrhea and whether or not the condition is primary or secondary seem to have little significance as to the results obtained.

OLIGOMENORRHEA

There were 39 cases in which the periods occurred irregularly at intervals greater than 5 weeks. Nineteen were relieved, 9 improved and 11 were failures.

Chart 3
OLIGOMENORRHEA, 39 CASES

	Relieved	Improved	Failures
Number of cases	19	9	11
Average age	26	23	26
Endocrine stigmata	5	3	6
Subsequent pregnancies	5	0	0
Average time observed, yrs.	2½	2¼	2

Irregular periods may represent a normal degree of ovarian function, the cycle being longer than that of the normal, or it may represent anovulatory menstruation. It is, on the whole, perhaps the mildest form of ovarian failure and from the results appears to offer the greatest probability of relief.

HYPOMENORRHEA

Scanty periods of 1 to 3 days' duration occurring at normal intervals were the complaint in 21 cases. Five were relieved, 7 improved and 9 failed to respond to treatment. There was no disturbance of the rhythm of flow in any. Three later developed symptoms of the menopause.

Chart 4

HYPOMENORRHEA, 21 CASES

	Relieved	Improved	Failures
Number of cases	5	7	9
Average age	26	28	33
Endocrine stigmata	1	2	2
Subsequent pregnancies	2	0	0
Average time observed, yrs.	4	1½	2

Scanty periods are difficult to evaluate. It has been our experience that the usual findings in such cases are normal hormone level and endometrial reaction, even in cases in which the flow lasts only one day. We do not know the cause of bleeding nor the mechanism for control of the amount of flow. The answer may lie in the responsiveness of the uterus or it may be an unknown factor, the bleeding factor. Scanty periods as the only complaint respond very poorly to any form of therapy.

OLIGOMENORRHEA AND HYPOMENORRHEA

There were 14 cases in which the periods were both irregular and scanty.

Chart 5

OLIGOMENORRHEA AND HYPOMENORRHEA, 14 CASES

	Relieved	Improved	Failures
Number of cases	4	6	4
Average age	33	32	30
Endocrine stigmata	3	1	2
Subsequent pregnancies	1	0	0
Average time observed, yrs.	2½	2	2

POLYMENORRHEA

There were 41 cases in which there was excessive bleeding. Twenty-one of these were relieved, 5 improved and 15 failed to respond. Of the failures 3 required a dilatation and curettage and radium to control the bleeding. One case in which bleeding could not be controlled came to operation several months later and chocolate cysts of the ovaries were found.

Functional bleeding as a rule represents a milder type of ovarian failure than amenorrhea, but more severe than oligomenorrhea and hypomenorrhea. In this condition there is follicular function to the point of excess, but corpus luteum function is either absent or deficient. Therapy must be directed toward producing luteinization of the follicle or supplying the deficient corpus luteum hormone. Control of bleeding, however, does not always indicate restoration of normal ovarian function.

Chart 6

POLYMENORRHEA, 41 CASES

	Relieved	Improved	Failures
Number of cases	21	5	15
Type of bleeding			
Prolonged and profuse	5	1	4
Too frequent	10	0	5
Acyclic	6	4	6
Average age	27	26	26
Endocrine stigmata	3	1	4
Subsequent pregnancies	3	0	0
Average time observed, yrs.	2	2½	2

ENDOCRINE STIGMATA

Under the term endocrine stigmata are included obesity, abnormal distribution of hair, abnormal body development as the infantile, masculine or eunuchoid type, and infantilism. They are significant primarily from the standpoint of prognosis.

Abnormal growth of hair alone, even of marked degree and of male distribution, seems to have little significance as far as ovarian function is concerned. We have seen repeatedly such patients who had normal ovarian function, conceived and bore normal children. When it occurs with symptoms of tumor of the pituitary, adrenals or ovary, it becomes significant. It occurred as the only complaint in 2 cases and in 5 cases with menstrual irregularities. In no instance was it affected by any form of therapy.

Abnormalities in body development are quite significant as they represent endocrine disturbances at an early age during development and growth of the bones, which disturbances may or may not have persisted into adult life. Quite often they are associated with menstrual irregularities and sterility. Their significance is demonstrated by the increase in incidence in the group who do not respond to treatment.

OBESITY

Obesity was present in 55 cases, 9 of whom had normal menstrual cycles and 46 had menstrual irregularities.

Obesity is fairly common in cases with menstrual abnormalities. The two seem to constitute a vicious cycle. It has been our experience, however, that relief of one often leads to im-

Chart 7

OBESITY, 55 CASES

	Relieved	Improved	Failures
Normal cycle, 9 cases			
Number of cases	5	2	2
Abnormal cycle, 46 cases			
Number of cases	20	18	8
Periods became regular	15	12	8
Total	35	20	10

provement in the other. Reduction of weight by diet alone often leads to improvement of menstrual function and, on the other hand, correction of menstrual irregularities makes reduction of weight easier. But weight cannot be reduced by endocrine therapy alone. Diet is the essential factor in all weight reduction.

DYSMENORRHEA

Painful periods was a complaint in 62 cases.

Chart 8

DYSMENORRHEA, 62 CASES

	Relieved	Improved	Failures
Number of cases	9	9	13
Average age	26	25	25
Endocrine stigmata	0	1	0
Subsequent pregnancies	1	1	3
Average time observed, yrs.	2½	1½	3
Cases with menstrual irregularities	17	8	6
Total number	26	17	19

Dysmenorrhea is of diverse etiology, which may or may not represent faulty ovarian function. The dysmenorrhea which accompanies irregularities of menstruation responds very well to treatment. Dysmenorrhea as the only complaint often fails to respond to any kind of treatment.

MENOPAUSE

There were 21 cases of menopause, 19 natural and 2 surgical. The complaints were typical, including hot flashes, nervousness, fatigue, mental depression, arthralgia and insomnia. All received irradiation of the pituitary at some time in the course of the treatment and all received estradiol benzoate by hypodermic.

Chart 9

MENOPAUSE, 21 CASES

	Relieved	Improved	Failures
Number of cases	11	9	1

In one case of surgical menopause, the hot flashes were so frequent and severe that they were not controlled by 50,000 international units of estrogenic hormone twice weekly. A course of 4 x-ray treatments at weekly intervals was given with no relief.

The symptoms of menopause can in most instances be completely controlled by administration of the estrogenic hormone. Irradiation given in conjunction with the ovarian hormone seems to hasten the alleviation of symptoms and shorten the duration of treatment. It may reduce the number of recurrences, but it does not completely prevent them.

STERILITY

Fifty-three patients, 20 with normal menstrual cycles and 33 with menstrual irregularities, received irradiation for sterility. Sixteen had some other factor as male infertility or closed tubes to account for the sterility. Nineteen conceived, 4 of whom aborted, and 4 developed symptoms of the menopause. Of the 19 who conceived, 5 had previously had anovulatory bleeding.

Chart 10

STERILITY

	Primary Sterility	Secondary Sterility
Regular periods, 20 cases		
Number	15	5
Pregnant	5*	3*
Contributory factors	8	0
Abnormal periods, 33 cases		
Number of cases	29	4
Pregnant	10**	1
Contributory factors	7	1

*One aborted.
**Two aborted.

Sterility is usually due to a combination of faults in both the male and female, but it may be due only to a failure of the endocrine glands concerned with the reproductive function in the female. This endocrine type of sterility may be associated with disturbances in the menstrual cycle or the periods may be apparently normal. The sterility is due to the fact that either an egg is not being extruded from the ovary each month, the so-called anovulatory type of menstruation; or it may be due to the fact that the lining of the uterus is improperly prepared to receive the fertilized ovum. Therapy directed toward stimulation of the ovary often overcomes these faults and makes pregnancy possible.

MISCELLANEOUS CASES

There were 20 patients in whom the complaints were not related to menstrual abnormalities, who were treated with irradiation. Complaints included headaches, nervousness and frigidity.

Headaches in which no organic basis for the condition could be found was the only complaint in 9 cases. One was relieved, 2 were improved and 6 showed no change. Headaches as a secondary complaint, exclusive of menopause cases, occurred in 18 cases. In 13 cases in which complete relief was obtained, the menstrual difficulties were also relieved. In the 5 cases in which there was no relief, there were no changes in the menstrual function.

Nervousness and fatigue are often the first symptoms of ovarian failure and are present to a more or less degree in practically all cases of frank ovarian failure. The majority of the patients treated experienced relief from these symptoms, often when there was no change in the menstrual status. Of the 2 cases in which nervousness of an extreme degree was the only complaint, 1 was relieved.

Frigidity is a common complaint associated with menstrual irregularities. With the return to normal function and increase in general well-being, libido often returns to normal. But in the 2 cases in which it was the only complaint, irradiation was not helpful.

Nymphomania was the complaint of a patient, aged 60. She received 22 irradiations to her pituitary, was relieved of her symptoms and showed no ill effects of the irradiations.

Double vision in one case was completely relieved by one irradiation. The patient had a low level of estrogenic substance and an excess of prolan in her urine, which suggested that the difficulty was due to a hyperfunction of the pituitary with swelling of the gland which caused pressure on the optic nerve.

Convulsions were the complaint in 3 cases with normal periods. Two showed slight improvement and 1 no change. Of 4 cases with abnormal cycles, 1 was relieved, 1 improved and 2 showed no change.

Abnormal growth of hair (2 cases) has been discussed.

ENDOMETRIAL BIOPSIES

Endometrial biopsies were done on 115 cases as a diagnostic procedure. The findings are summarized in *Chart 11.*

Chart 11

ENDOMETRIAL BIOPSIES AS DIAGNOSTIC PROCEDURE, 115 CASES

Secretory endometria		67
Normal	25	
Abnormal	42	
Follicular type		48
Persistent	18	
Anovulatory	23	
Atrophic	8	

There were 25 cases, or 22 per cent, with a secretory reaction apparently normal in structure. These included: 4 cases of sterility, 2 of which became pregnant; 8 cases of oligomenorrhea, 7 of which the cycles were made to occur more frequently; 4 hypomenorrhea, only 2 of which improved; 6 cases of dysmenorrhea, 4 of which improved; and 2 obesities, 1 of which improved, and 1 with no breast development, in which no change was induced.

There were 42 cases with an abnormally developed secretory reaction. Forty-eight cases had follicular endometrium, 23 of whom represented anovulatory menstruation. As we have discussed the relation of the endometrial findings to the symptoms more fully elsewhere,[10] we will not go into it further now than to say that 78 per cent of the cases treated had sufficient disturbance of ovarian function to be reflected in the endometrium. This is quite high when it is considered that cases complaining of only subjective symptoms as nervousness, headaches and sterilities with apparently normal periods are included.

The more significant use of the biopsy, in relation to this report, are the 32 cases in which it was used as a check on the result of therapy. These cases are classified as to the original endometrial reaction and the reaction after treatment.

Chart 12

Endometrium	Period Observed	Complaint		Results
Normal secretory	14 mos.	Hypomenorrhea	1	Relieved
Remained	5 mos.	Hypomenorrhea	1	Improved
Normal secretory	11 mos.	Hypomenorrhea	1	Failure
	2 yrs.	Small breasts	1	Failure
Abnormal secretory		Headaches	1	Relieved
Became	5 mos.	Polymenorrhea	2	Relieved
Normal secretory		Hypomenorrhea	1	Relieved
		Dysmenorrhea	1	Relieved
Abnormal secretory	6 mos., 4	Sterility	2	Relieved
Remained	1 yr., 2	Sterility	4	Failure
Abnormal secretory	18 mos., 2	Convulsions	1	Failure
		Dysmenorrhea	1	Failure

Chart 13

Endometrium	Period Observed	Complaint		Clinical Results
Follicular	6 mos.,	Polymenorrhea	1	Improved
Remained	1 yr., 3	Oligomenorrhea	1	Failure
Follicular		Polymenorrhea	3	Failure
Follicular	6 mos., 2	Sterility	2	Pregnant, aborted
Became	1 yr., 1	Sterility	2	Failure
Abnormal secretory	18 mos., 2	Polymenorrhea	1	Improved
Follicular	6 mos., 3	Polymenorrhea	3	Relieved
Became	1 yr., 2	Sterility	1	Relieved
Normal secretory		Sterility	1	Failure

There were 4 patients who had a normal secretory reaction which remained so throughout the study. In a case of hypomenorrhea, 4 biopsies were taken over a period of 14 months. The patient received 5 pituitary and 1 pelvic irradiation and was relieved. A second case of hypomenorrhea in which 2 biopsies were taken over 5 months received 4 pituitary irradiations and was improved. A hypomenorrhea in which 4 biopsies were taken over a period of 11 months received 4 pituitary irradiations and was not improved. In the cases with small breasts, 3 biopsies were taken over a period of two years. There was no change.

There were 8 cases of abnormal secretory premenstrual endometria which, checked at intervals of 6 to 18 months, still showed an abnormal secretory reaction. This included 6 sterilities, 2 of whom later became pregnant and one case each of convulsion and dysmenorrhea which obtained no relief.

Mrs. S. B., aged 25, married 5 years, was sterile with scanty periods. Biopsies taken at intervals of 4 months for 16 months showed no change from the original poorly developed secretory reaction. No pregnancy occurred.

There were 5 cases in which an abnormal secretory was converted to a normal secretory reaction. These included a case of headache, 2 of prolonged bleeding, 1 hypomenorrhea and 1 dysmenorrhea. All were relieved of their symptoms.

Mrs. B. H., aged 21, had had periods which lasted 2 to 3 weeks for the preceding three months. First biopsy showed abnormal secretory reaction of "irregular shedding" type. She was completely relieved and is now pregnant.

There were 5 cases in which a follicular type remained follicular after treatment. Two were checked after 6 months and 3 after 1 year. Three cases of polymenorrhea and 1 of oligomenorrhea showed no clinical improvement in this time, while 1 polymenorrhea was relieved.

Mrs. G. H., aged 34, married 9 years, was sterile. She was first seen after 9 months of amenorrhea. She bled after the first biopsy and bleeding recurred fairly regularly at two-week intervals, but occasionally 6 to 8 weeks of amenorrhea occurred. Each of six biopsies taken over a period of a year showed an early follicular reaction.

A follicular endometrium was converted to a secretory reaction which was not normal in structure in 5 cases. Two of these were followed for 6 months, 1 for 1 year and 2 for 18 months. There were 4 sterilities, 2 of which conceived but aborted, and 1 polymenorrhea, which was improved.

Mrs. S. W., aged 30, married 7 years, sterile, had severe dysmenorrhea. First biopsy showed follicular hyperplasia. Biopsy taken 5 months and 12 months later showed abnormal secretory reaction. Six months later pregnancy occurred, which was aborted at 2 months.

A follicular endometrium was converted to a normal secretory in 5 cases. Three of these were followed 6 months and 2 one year. Three cases of polymenorrhea were relieved, one sterility became pregnant and one sterility failed to conceive.

Mrs. L. A., aged 26, married 4 years, was sterile. First biopsy showed follicular hyperplasia. Second biopsy 2 months later showed normal secretory phase. Her last normal period occurred 4 months after the last treatment.

SUMMARY

(1) Two hundred forty-three cases have been treated by irradiation of the pituitary region and organotherapy for disorders related to the menstrual function.

(2) Cases were observed for six months to nine years after treatment, the average length of time being two years. Only those cases which were restored to normal function and remained so were classified as "relieved." Those included under "improved" included also those relieved for a while with partial relapses. "Failures" also included cases which had responded somewhat, but had complete relapses.

(3) Amenorrhea responded fairly well to treatment. Fifty-six per cent were relieved and 44 per cent failed to respond to treatment.

(4) There is apparently a difference in the underlying disturbed physiology of irregular, infrequent periods and scanty periods. The former may represent normal ovarian function in longer and irregular cycles or actual ovarian deficiency. Hypomenorrhea may be ovarian in

origin, but more often such function is normal. This suggests that other factors as uterine unresponsiveness or some other as yet unknown factors are the causative agents. This difference is clearly reflected in the response to treatment of the two groups. Irregular periods were relieved or improved in 77 per cent, while only 57 per cent of the scanty periods showed such response. The combination of scanty and irregular periods were relieved or improved in 71 per cent of the cases.

(5) Functional bleeding, which represents faulty corpus luteum function, usually with a relative or actual excess follicular activity, responds fairly satisfactorily to treatment. In this series, 63 per cent were relieved or improved. In the failures are included cases in which such measures as small doses of radium had to be resorted to for control of the hemorrhage.

(6) Dysmenorrhea is of diverse etiology and therefore cannot be treated successfully by one method. Pain associated with regular periods as compared to that which accompanies menstrual irregularities is more resistant to treatment. In this series relief or improvement was obtained in only 58 per cent of the former, while 80 per cent of the latter responded to treatment.

(7) Sterility was a complaint in 53 cases treated, but 16 of these had other contributory factors as closed tubes or male infertility. Pregnancies occurred in 19, or 45 per cent, of the cases which were purely endocrinal in origin, 4 of whom aborted.

(8) Menopausal symptoms are usually easily controlled by the estrogenic hormone. The addition of irradiation may be helpful in hastening the alleviation of symptoms and reducing the period of organotherapy, but it does not absolutely prevent recurrences.

(9) Obesity and menstrual irregularities are often concomitant. Relief of one often leads to improvement of the other, but all obesities require diet as the fundamental element of treatment.

(10) Subjective symptoms as nervousness, headaches and frigidity, when they occur with menstrual irregularities, are usually relieved with the restoration of a normal menstrual function.

(11) Regular menstrual cycles were not disturbed by this form of therapy. This would seem to indicate that, regardless of its effectiveness, irradiation is not harmful.

(12) Endometrial biopsies, taken repeatedly in 32 cases, indicated that 10 cases previously abnormal were restored to normal function, while 5 were improved. None showed regression in ovarian function.

CONCLUSION

Functional menstrual irregularities can be treated satisfactorily with a combination of organotherapy and irradiation of the pituitary region. From this study of the results obtained over a period of time we cannot say which factor, irradiation or organotherapy, is the most important.

Whether with the years irradiation will prove to be the outstanding form of therapy for pituitary failure we cannot say. At the time when glandular products were relatively impotent it served a useful purpose. With the rapid advances in research on the mechanism of the menstrual function and the addition of pure and potent products to our armamentarium, the treat-

Chart 14

SUMMARY OF RESULTS OBTAINED

	Number of Cases	Per Cent Relieved	Per Cent Improved	Total Per Cent Improved
Amenorrhea	27	22.3	33.3	56
Oligomenorrhea	39	48.5	28.3	77
Hypomenorrhea	21	23.9	33.3	57
Oligomenorrhea and hypomenorrhea	14	28.5	42.8	71
Polymenorrhea	41	51.2	12.2	63
Dysmenorrhea	62	41.9	27.4	70
Normal periods	31	29	29	58
Abnormal periods	31	54.8	25.8	80
Sterility	53	32		32
Normal periods	20	30		30
Abnormal periods	33	33		33

ment of such disorders may some day become simple. But until that day arrives, the use of irradiation with the available endocrine products seems to be justified.

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DISCUSSION (*Abstract*)

Dr. J. Cash King, Memphis, Tenn.—This problem of pituitary irradiation in menstrual disorders is one very close to me just now. The photomicrographs of endometrial biopsies and vaginal spreads shown by Dr. Kotz demonstrating the changes that follow pituitary treatment present work which we have all been anxious to see. Having recently reviewed and reported on 75 cases, I am very much impressed by the results the essayists have obtained.

In oligomenorrhea, amenorrhea and menorrhagia, our results have been quite similar to his. Certainly one cannot help being enthusiastic about the results with this form of therapy when accurate diagnosis is made and the case is well selected for treatment.

I do not think it harmful to theorize a little as to how the radiation brings about the end result: (1) Wolfe and others say that antihormonal substances as well as hormones are produced by the glands of internal secretion. If an overproduction of antihormonal substance is a factor in the production of this dysfunction, it may be that the radiation neutralizes this overproduction of antibodies. (2) Another possibility is that these small doses increase the vascularity to the gland permitting a better inflow of raw materials as well as a better output of the finished products, hormones, from the gland. (3) The irradiation could have a beneficial effect upon any inflammatory process that might disturb the gland function.

I want to compliment the essayist upon recommending that we use all of the useful therapeutic agents in the management of these cases rather than rely entirely upon pituitary radiation. Certainly the cases with hypothyroid function must have substitutional therapy before complete correction can be obtained. Dr. Kotz's thorough work and report are valuable additions to the literature.

Dr. Franklin B. Bogart, Chattanooga, Tenn.—We certainly do not definitely know the exact mode of action of x-rays on the pituitary gland in these groups of cases. The dose of x-rays that is usually given is not large enough to produce a destructive action, and radiologists hesitate to believe that irradiation will produce true cell stimulation.

A note of warning should be sounded in regard to the selection of cases for pituitary irradiation. If the radiologist is working with a group of physicians, where the cases are carefully gone over, and where one or two gynecologists or internists are selecting the cases, good results will probably be obtained. In an open staff hospital and in private practice, cases are apt to be referred with definite instruction for irradiation to the pituitary or to the ovaries, or to both in many cases that present bizarre and confusing syndromes, in the blind hope that irradiation may in some way aid in bringing relief to the patient. Many such cases are unsuited for pituitary or ovarian irradiation.

Organotherapy should certainly be given a trial before irradiation is resorted to, or they should be combined, as has been done by Dr. Kotz.

In reading the literature, considerable variation is noted in the dosage advocated. Most men use a small dose and our dosage has continued to be small and has not been changed since our report before this section a year ago.

Dr. Edwin C. Ernst, St. Louis, Mo.—The essayist spoke of large doses and small doses in the radiation treatment of pituitary dysfunction. Were the doses described measured on the skin, in air, or within the deeper tissue structures? I think it is very important to those who may be listening, not having the opportunity of reading the paper for some time. No doubt these facts are adequately presented in the published report. It is very important not to give a stimulating dose without knowing actually what reaches the pituitary region, since the sizes, shapes, and densities of the skull present many variables.

Unless the dose is accurately described, the same amount of radiation applied to each part may produce widely different pituitary effects because of the different tissue roentgen absorptions, due to the physical differences of distance and skull table opacities.

Dr. Kotz (*closing*)—Several questions are often asked pertaining to the use of irradiation of the pituitary gland. One is, "What is the effect on the babies born to those women who have had irradiation therapy?" So far as we can determine, there is none. We have had a fair number of such cases and the babies appear normal in every respect.

Another question is, "What is the mechanism of its action?" That we do not know. The objection that such therapy is empirical should not limit its use. We have very few specifics in medicine today and yet many drugs are used.

As to the harmful effects of irradiation, we have approached the problem by three methods: questionnaires sent to patients, endometrial biopsies and animal experimentation. The first two are incorporated in this paper. The last is to be reported later. From none of these has there been any evidence of damage as the result of irradiation.

Dr. Bogart has stressed an important point and that is the proper selection of cases upon which irradiation is to be used. All cases should be examined by a competent gynecologist before being referred for therapy.

Someone has asked the dosage used. We employ two methods; in one, 102 r is given at weekly intervals, and in the second, 130 r every three weeks, each for three to four treatments. In some cases, irradiation of the ovaries is used in conjunction with irradiation to the pituitary, but this method is limited to those cases in which enlargement of the ovaries is present.

PELVICEPHALOGRAPHY*

AN ANALYSIS OF 503 SELECTED CASES

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Ball's[1] method of pelvicephalography, perhaps because of its simplicity, has attained particularly wide popularity among the various technics which have been devised for the application of roentgenology to obstetrics. Impressions as to its accuracy and clinical value, however, are widely conflicting, and a just estimate of its merits can be arrived at only by the study of large series of cases from both the clinical and the radiologic point of view. Such a study is reported herewith. Since only three physicians, a radiologist and two obstetricians were engaged in it, the personal equation is eliminated as far as possible, and, in addition, a consistent endeavor was made to preserve an impartial point of view in the analysis and to avoid undue and unwarranted enthusiasm.

The 503 cases which make up this series were chosen from the more than 6,000 deliveries conducted at Charity Hospital of Louisiana at New Orleans during the fifteen-month period ending October 1, 1939. The figures are frankly overweighted; although the series includes a large number of normal cases in which x-ray examination was made to confirm normal clinical findings or for strictly control purposes. It also includes nearly all the patients seen during the period, in whom dystocia was due to fetopelvic disproportion evident or suspected, all patients with abnormalities of the bony pelvis, and all patients in whom labor was unduly prolonged. One hundred ninety-one of the 503 patients were white and 312 colored. Three hundred and sixty-two were primiparae and the parity in the other cases ranged from two to ten. Four hundred and sixty-five presentations were vertex and 38 breech.

TECHNIC

Pelvicephalography by Ball's method is performed as follows: two exposures are taken. For the anteroposterior view the patient lies supine, with the median plane over the center line of the Potter-Bucky diaphragm. The central ray is projected vertically through a point midway between the antero-inferior iliac spines. For the lateral view she lies on one side or the other, with the median plane over the center line of the diaphragm. The central ray is projected vertically through the greater trochanter. A single exposure is made in each position, using 200 ma. seconds, 36-inch anode film distance, and approximately 75-85 kilovolts.

Appropriate corrections are necessary for the magnification which is always present to some degree, depending upon the anode film distance and the object film distance. The object film distance is determined from the lateral view for the anteroposterior view, and from the anteroposterior view for the lateral view. Correction for magnification is made by a mechanical calculator devised by Ball, by which means the corrected pelvic diameters and fetal head circumference are secured. From these measurements the volume capacity of the pelvis and the volume of the fetal head can be calculated and the fetopelvic relationship determined. It is also possible, with the mean circumference of the fetal head at hand, to determine the weight of the child by reference to a standard chart also prepared by Ball.

ARCHITECTURE

Pelvicephalography is intended primarily to provide information concerning pelvic architecture, pelvic measurements, fetal head measurements and weight, and cephalopelvic proportions. In addition, careful scrutiny of the films will reveal valuable information as to the presentation, position and attitude of the fetus, as well as the possible presence of a dead fetus, a monster, or a multiple pregnancy. These data sometimes prove of even greater clinical significance than the information provided by simple volumetric comparisons of the fetal head and the maternal pelvis.

A study of pelvic structures as revealed by the films furnishes the basis for the classification of the various types of pelvis and also readily demonstrates variations in architecture which may be difficult to determine by clinical methods. On the other hand, although certain abnormalities of pelvic architecture are commonly associated with dystocia and a knowledge of the type of pelvis present often supplies a useful warning, too much reliance cannot be

*Received for publication January 31, 1940.

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placed upon pelvic architecture *per se*. Radiologic data should be used only in conjunction with pelvimetry and fetopelvic relationship as the basis for a prediction of possible bony dystocia in labor.

The anteroposterior view supplies information as to the shape of the inlet and the prominence of the ischial spines. For practical purposes we have followed Thoms' classification of pelvic types, which is based on the shape of the inlet and includes the following divisions:

Platypellic, in which the transverse diameter of the inlet is more than 3 cm. greater than the true conjugate.

Brachypellic, in which the transverse diameter of the inlet is 1-3 cm. greater than the true conjugate.

Mesatipellic, in which the transverse diameter is equal to or not more than 1 cm. greater than the true conjugate.

Dolichopellic, in which the transverse diameter is less than the true conjugate.

The incidence of the various types of pelves in this series according to Thoms' classification is set forth in *Table 1*, from which it will be seen that the brachypellic type was most frequent (48.1 per cent) and the dolichopellic type the least frequent (8.9 per cent).

Table 1

DISTRIBUTION OF PELVIC TYPES IN 503 PREGNANT WOMEN STUDIED BY BALL PELVICEPHALOGRAPHY

Type Pelvis	White	Percentage	Colored	Percentage	Total	Percentage
Brachypellic	75	39.0	167	53.5	242	48.1
Mesatipellic	85	44.5	80	25.6	165	32.9
Platypellic	10	5.5	41	13.2	51	11.1
Dolichopellic	21	11.0	24	7.7	45	8.9
Total	191	38.0	312	62.0	503	100.0

The racial distribution of the various types of pelves differs from the distribution of the total series. In the 312 colored cases (62.0 per cent of the total) the incidence of the platypellic type was 13.2 per cent, as compared with an incidence of 5.5 per cent in the 191 white cases (38.0 per cent of the total). The mesatipellic type was present in 25.6 per cent of the negro women and the dolichopellic type in 7.7 per cent, as compared with 44.5 per cent and 11.0 per cent, respectively, of the white women. These racial differences are the more significant because the distribution of the various types of pelves among the white women is similar to the distribution reported from Northern clinics. Whether these differences are entirely racial in origin or are due to differences in diets and other causes we are not prepared to say.

Prominent ischial spines are not so important in themselves as in conjunction with other pelvic diameters. Patients who have prominent spines but whose pelvic measurements are otherwise adequate are likely, other things being equal, to deliver without difficulty. On the other hand, dystocia is to be anticipated in patients with prominent spines when the measurements of the transverse diameter of the midplane are diminished and posterior pelvic compensation is inadequate. These generalizations were borne out in this series. Dystocia occurred in 16 of the 20 patients whose ischial spines were prominent and whose bispinous diameters were small, although 24 other patients with prominent spines but otherwise normal measurements had uncomplicated labors.

Information as to the contour, shape and position of the sacrum is derived from the lateral film. These are factors which determine to a large extent the space in the posterior pelvis and therefore the possible degree of compensation for small measurements in the midplane. The sacrum was flat and convergent in 23 of these 503 cases and flat and divergent in 38. A prominent coccyx with anterior angulation and ankylosis at the sacrococcygeal articulation was present in 33 instances, these being abnormalities which are of no great significance in operative delivery per vaginum, though they may hinder natural delivery. The high assimilation type of pelvis was present in three instances, and the series also included two instances of dwarfism, three of deformity of the spinal column, five of old traumatic fractures of the pelvis, and one of chronic osteomyelitis of the hip joint. In most of these cases the history or physical findings suggested the presence of the pelvic abnormality, but the roentgenographic confirmation was of unquestioned value.

PELVIMETRY

Of the essential measurements which serve as guides to the amount of space available in the birth canal, some can be secured easily and accurately by clinical means, and roentgenography merely verifies the clinical data. On the other hand, some cannot be obtained directly,

but must be estimated, and their accuracy is dependent upon the experience and care of the physician making the examination. This personal equation is eliminated when roentgen pelvimetry is employed, and a highly accurate means of securing direct measurements of all the pelvic diameters is thus afforded.

The pelvic inlet is bounded anteriorly by the upper border of the posterior surface of the symphysis pubis, laterally by the iliopectineal lines, and posteriorly by the upper border of the first sacral vertebra. It has two important diameters, the transverse, which can be measured only by x-ray, and the anteroposterior or true conjugate. This diameter can usually be determined accurately by obtaining the diagonal conjugate by palpation and subtracting from this measurement approximately 1.5 cm. for the height, thickness and inclination of the pelvis. In this series the true conjugate was less than the transverse diameter in 91.1 per cent of the cases, and racial differences again are evident. The average true conjugate was 11.4 cm. and the average transverse diameter 12.1 cm. in the 191 white patients, as compared with 10.8 and 12.4 cm., respectively, in the negro cases. In 59 negro patients and 21 white patients the true conjugate was less than 10 cm., yet dystocia occurred in 67 per cent (14) of the white cases as compared with only 34 per cent (20) of the negro cases. The different incidence of dystocia in the two races, in spite of the apparently similar pelvic space, is readily explained. The small pelves of negro women are frequently compensated for by other factors: the negro baby has a smaller and more moldable head, the uterine mechanism is more forceful, and the threshold of pain seems to be higher, so that the negro parturient cooperates with the physician more readily than does her white sister. In this series the average weight of the colored babies was 7.5 pounds, as compared with 8.7 pounds for the white babies, the figures being somewhat higher than normal[2] because the series includes an undue proportion of large children.

The midplane extends from the lower border of the symphysis pubis through the ischial spines posteriorly to the junction of the fourth and fifth sacral vertebrae. It has two important diameters, the transverse, which is the distance between the ischial spines, and the posterior sagittal, which is the distance from the midpoint of the transverse diameter to the junction of the fourth and fifth sacral vertebrae. Both can be estimated only clinically, but can be measured accurately by x-ray, which is a distinct advantage, for the former indicates the space available in the transverse diameter of the midplane and the latter the posterior pelvic compensation. It has been our experience that if the sum of the two diameters of the midplane is less than 13.5 cm., as it was in 36 cases in this series, bony dystocia in the midplane is likely to occur, as it did in 22 (61.1 per cent) of these cases. Racial differences again are evident. The transverse diameter averaged 10.6 cm. and the posterior sagittal diameter 4.9 cm. in the white women as compared with 11.1 cm. and 4.4 cm., respectively, in the negro women. The small posterior sagittal midplane measurements which are rather frequent in negro women because of the high incidence of flat sacra are thus partially compensated for by large transverse diameters.

We do not advocate routine determination of the outlet (bituberous and posterior sagittal) diameters by x-ray. They can be adequately measured clinically and additional x-ray exposures would be necessary to secure them. Furthermore, with the exception of the transverse and posterior sagittal measurements of the outlet, external pelvimetry has often proven not only valueless, but actually misleading. In this series the average bituberous diameter was 9.8 cm. in the white and 10.0 cm. in the negro women and the average posterior sagittal diameters were respectively 7.0 cm. and 6.4 cm.

FETOMETRY

Fetometry by the Ball method is performed by measuring the mean circumference of the fetal head and applying this measurement to Ball's chart, from which the approximate weight of the fetus can be obtained. The fetal age is determined from the estimated weight. Fetometry, however, is by no means so accurate as is pelvimetry, and it is considerably less accurate in breech than in vertex presentation. In the 38 cases of breech presentation in this series the average error in the estimation of fetal weight at term was 0.92 pounds, against an error of 0.58 pounds in 465 vertex presentations. Even in the vertex cases, in which the estimates were reasonably accurate at term, the errors at six to eight months ranged from one to two pounds or more, being proportionately greater the younger the fetus. The errors are easily explained by the embryologic fact that in the last trimester of pregnancy the fetal head enlarges relatively slowly in comparison with the increase

in body weight. They are nonetheless unfortunate, for a knowledge of fetal weight from the twenty-eighth to the thirty-eighth week of gestation would be of real value to the clinician, especially when the viability of the child is in question. In line with Ball's own suggestion we are at present endeavoring to prepare a large series of fetal head-fetal weight correlations at the various weeks of gestation. When adequate series of this sort are available for reference, errors will not be so likely to occur as at present and fetometry will become correspondingly more accurate.

PELVICEPHALOGRAPHY

In the Ball method of pelvicephalography the volume of the fetal head, which is estimated from the mean circumference, is compared first with the volume capacity of the pelvic inlet, which is estimated from the true conjugate, and then with the volume capacity of the midplane, which is estimated from the transverse diameter of the midplane. A volumetric comparison between the fetal cranium and the pelvic inlet and the midplane is thus possible. Two warnings, however, are necessary. The first is that neither the pelvic inlet nor the fetal head are perfect spheres, one of which fits exactly into the other. The second is that the fetal head changes shape during labor. The fetal cranium *in utero* is normally spheroid and the circumference can be measured with reasonable accuracy at two right angle planes, the mean measurement being used to calculate the cephalic volume. Once molding has occurred, these facts no longer hold, for the contour of the head becomes more or less ovoid. For these reasons obstetric roentgenography furnishes more accurate information at the onset of labor or shortly thereafter rather than several weeks before term or after labor is considerably advanced.

According to Ball, if the volume of the fetal head exceeds the volume capacity of the inlet by more than 150 milliliters dystocia can be predicted at this level. If the fetal head volume is more than 250 milliliters greater than the volume capacity of the midplane, dystocia can be predicted at this level. We have employed somewhat different standards and do not predict dystocia unless the head volume exceeds the volume capacity of the inlet by more than 200 milliliters. As *Table 2* shows, dystocia occurred in four-fifths of the 45 cases having such a ratio, against slightly more than a third of the 52 cases in which the ratio was 150-200 milliliters. Dystocia due to disproportion at the pelvic inlet was encountered ten times as frequently in the group of cases in which it was estimated that the fetal head volume was greater than the volume capacity of the inlet (37.0 per cent) as in those in which the converse was true (4.2 per cent). Delivery by cesarean section was necessary in 70 of the 80 cases (*Table 2*) in which dystocia occurred at the inlet, and craniotomy was done in the 10 other cases.

Table 2

INLET PELVICEPHALOGRAPHY IN 465 VERTEX PRESENTATIONS

Disproportion in Milliliters	Number Cases	Dystocia	Percentage
(A) FETAL HEAD VOLUME GREATER THAN VOLUME CAPACITY OF INLET			
Over 200	45	36	80.0
150-200	52	21	40.4
1-150	87	11	12.6
Subtotal	184	68	37.0
(B) FETAL HEAD VOLUME LESS THAN VOLUME CAPACITY OF INLET			
Over 100	63	0	0
1-100	218	12	5.5
Subtotal	281	12	4.2
Total	465	80	17.2

Dystocia at the midplane occurred in 44 of the 385 vertex presentations remaining after the 80 cases of inlet dystocia just described are subtracted from the total number (465, *Table 3*). Here again it is demonstrated with striking emphasis that bony dystocia is encountered much more frequently in those cases in which the calculated volume of the fetal head is greater than the volume capacity of the pelvis. The difficulty is not always a simple midplane dystocia, but a combination of a borderline inlet and an abnormal midplane. This was the situation in 21 of the 44 cases in which midplane dystocia occurred. Furthermore, midplane pelvicephalometry, as has already been emphasized, should not be used for prognosis without due regard for posterior pelvic compensation. Dystocia occurred in 75.2 per cent of the cases in which such compensation was inadequate against 57.8 per cent of the cases in which it was adequate.

In most of the 38 breech presentations the correlation between the radiologic findings and the clinical course was not sufficiently close to

Table 3

MIDPLANE PELVICEPHALOGRAPHY IN 385 VERTEX PRESENTATIONS

(A) FETAL HEAD VOLUME GREATER THAN VOLUME CAPACITY OF MIDPLANE

Disproportion in Milliliters	With Adequate Posterior Pelvic Compensation			With Inadequate Posterior Pelvic Compensation		
	Number Cases	Dystocia	Percentage	Number Cases	Dystocia	Percentage
Over 250	11	7	63.6	18	14	77.7
1-250	17	9	52.0	11	8	72.7
Subtotal	28	16	57.8	29	22	75.2
(B) FETAL HEAD VOLUME LESS THAN VOLUME CAPACITY OF MIDPLANE						
Over 100	112	2	1.7	2	0	0
1-100	209	4	1.9	5	0	0
Subtotal	321	6	1.8	7	0	0
Total	349	22	6.3	36	22	61.1

establish the method as of any great prognostic value. This is not difficult to explain. In breech cases the magnification of the fetal head is greater than in vertex cases, and the lack of a fixed point for correction accounts for the distortion of the head size. In 21 of the 38 cases the calculated fetal head volume exceeded the volume capacity of the inlet by more than 200 milliliters, yet dystocia occurred in only two instances, in both of which, however, craniotomy was necessary. Dystocia did not occur at the midplane in any breech case, although the calculated fetal head volume was estimated to be 200 milliliters greater than the volume capacity of the midplane in 29 cases, in seven of which the pelvic measurements were smaller than normal.

It should be emphasized that in the discussion of the value of pelvicephalography as based on the correctness of the prognostication of dystocia, other causes of difficult labor have been eliminated, including malpresentations, uterine inertia, soft tissue dystocia, and similar tangible and intangible factors.

SUMMARY AND CONCLUSIONS

(1) The Ball method of pelvicephalography affords a simple and accurate means of securing information concerning pelvic architecture, pelvimetry, fetometry and pelvicephalography in vertex presentations, but is often inaccurate and misleading in breech presentations.

(2) Measurements of the pelvic inlet and outlet can be secured clinically, and roentgen pelvimetry merely supplies confirmation. The midplane measurements, however, can be secured only by x-ray. A difficult or dangerous delivery can be anticipated in most cases in which the true conjugate is less than 9 cm. and in which the sum of the two diameters of the midplane is less than 13.5 cm. Dystocia is more likely to occur in those cases in which the calculated volume of the fetal head is greater than the volume capacity of both the inlet and the midplane.

(3) The data obtained by combining a survey of gross pelvic architecture with precise pelvimetry permits a classification of pelvic type which may be of prognostic aid. Accurate information of this sort is essential for the proper conduct of labor and is particularly helpful if operative intervention should prove necessary.

(4) Radiologic results must naturally be combined with clinical judgment, for it is entirely irrational to expect to predict the outcome of a variable human process on the basis of purely mechanical estimation. Labor is dependent upon conditions other than the comparative size of the fetal head and the bony pelvis, and x-ray studies cannot supply the sound obstetric judgment required to cope with these factors, many of which are intangible. When the proper allowance has been made for these considerations, the Ball method offers warning signals which, although they should never be accepted as absolute in the management of labor, are at least monitory.

(5) These conclusions are based upon and borne out by the results of pelvicephalography by the Ball method in 503 obstetric cases.

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TUMORS COMPLICATING PREGNANCY*

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Since pregnancy occurs usually during the early part as well as at the most healthy period of a woman's life, one naturally expects very few neoplasms, either benign or malignant. A review of the literature reveals such a supposition to be true as Schauta, Pinard, and Pierson found fibromyomata uteri to be present in 0.1 to 0.7 per cent in a large series of cases. From this it may be concluded that the obstetrician will, at most, encounter one or two cases per hundred in which tumors are present. However, with continued advancement in the field of endocrinology and by improved treatment of sterility, an increasing number of pregnancies will occur among older women. In Schauta's series of cases, three-fourths of the patients in whom fibroids were present, were past thirty years of age. One may expect an increasing number of cases of pregnancy to be complicated by tumors. For the sake of brevity, cervical polyps, hydatid moles, vaginal cysts and malignancies of the reproductive organs will not be included in this discussion. Neither will very small solitary ovarian cysts nor small uterine fibroids be considered as complicating factors of pregnancy. Our remarks will be limited to a consideration of the commonest types of tumors complicating pregnancy, namely myomata, cystoma and fibroma. Also a few cases, because of their clinical interest as well as perplexing symptoms, will be presented.

GENERAL CONSIDERATIONS

Fibromyomata are the commonest tumors complicating pregnancy. They may produce complications which require the highest degree of obstetrical judgment. They may affect fertility, pregnancy, labor, and the puerperium. In a critical study of 4,330 deliveries of private patients of the authors, and approximately 200 cases seen in consultation, only 47 cases were complicated by tumors, or approximately 1 per cent. Fibroids of the uterus accounted for 36 cases, or approximately 77 per cent of this series.

*Read in Section on Gynecology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

FIBROMYOMATA UTERI

According to Watson,[1] there is an average sterility among women of 10-15 per cent compared with 30 per cent in cases with fibroids. It is believed that women who have had children are less liable to have fibroids than those who have had none. In only 8 cases out of the 36 pregnancies with fibroids were the patients under 30 years of age. In only 3 cases were the patients under 25 years of age. Of the 28 patients who were past 30 years of age, the great majority were between 32 and 38 years. There was only one patient over forty years of age. Therefore, from this small series of cases, it may be stated that if fibroids are associated with pregnancy, they are most likely to be found in patients about 35 years of age. It was also surprising that in only 10 cases did we find pregnancy, labor and the puerperium to be essentially normal. In eight cases it was deemed wise to perform a cesarean section at term and remove the uterus. In only two cases was a myomectomy performed at the time of the cesarean. In two cases myomectomy was performed in early pregnancy and this caused no disturbance to the existing pregnancy. Among five cases in which a classical cesarean was performed, the uterus had to be removed before two years had elapsed in two, because of severe symptoms due to the tumor. In only one case was pregnancy interrupted and this was done by hysterectomy at 4½ months because of bleeding, marked loss of weight, and severe vomiting. There were four normal deliveries of patients who continued to bleed and have marked pain for eight to ten weeks postpartum in spite of the usual treatment. It became necessary to remove the uterus in three of these cases and it was found that fibroids had undergone necrosis and red degeneration. One such case was treated successfully with roentgen therapy, but this patient when last seen three years later was having symptoms of pressure due to the fibroids. There was only one case in which the placenta had to be removed manually. Three cases had severe postpartum bleeding and a brief summary of a fatal case is presented.

Case 2599.—Mrs. B. D., aged 38, was seen in consultation about 40 minutes after a rather rapid labor of four hours. She was a para 3 and during this pregnancy had suffered with severe pains in the lower abdomen requiring opiates for relief. There were several large fibroids present. This patient had been advised to have a cesarean section and hysterectomy but she refused. No anemia, hypertension, nor albuminuria during pregnancy was found. After a spontaneous delivery with

no analgesic and very little ether, the patient bled rather freely following expulsion of the placenta, and almost immediately the radial pulse became imperceptible and the blood pressure unobtainable. Uterine massage, posterior pituitary extract, ergot, uterine and vaginal packing failed to check bleeding. There were no cervical or vaginal lacerations. She was placed in Trendelenberg position, and 1000 c. c. of 5 per cent glucose were administered immediately while her husband was being matched for transfusion. The operating room was in readiness for hysterectomy but the condition of the patient did not warrant a surgical procedure. The patient expired during the transfusion after 350 c. c. of blood had been given. The bleeding, while never severe, was constant and was never checked. Autopsy showed an intramural fibroid which measured about 10 cm. in diameter, situated in the posterior wall of the uterus.

The value of having every patient who has a fibroid typed and matched for transfusion before delivery is definitely illustrated by this case. It also shows that fibroids may cause fatal postpartum hemorrhage.

Tiber and Turkel[2] say that sterility is dependent upon the site of the tumor, the submucous causing the greatest per cent of sterility while the subserous causes the least. The same findings hold true for cause of abortion. Watson reports 71 early or late abortions in 157 cases of fibroids. Necrobiosis or red degeneration is by far the most frequent complication and occurs more commonly during the puerperium. The symptoms are pain and tenderness over the site of the tumor and low grade fever rarely over 101° unless there is secondary infection. Campbell[3] reported 142 cases of fibroids, 82 of which presented complications during pregnancy, labor, or the puerperium. Three-fourths of these tumors removed during pregnancy showed necrosis. Mussey and Hardwick[4] report 297 cases of pregnancy with myomata, 97 of which were of clinical significance. There were 32 myomectomies performed on these 97 cases and 21 cases showed alarming symptoms of necrobiosis. During late pregnancy these tumors predispose to premature labor, red degeneration, twisted pedicle, and abnormal presentation.

Tumors which have been unsuspected may first make their appearance during the last trimester, for they are projected as distinct knobs as the uterus thins out. The ability of the abdomen to accommodate a large fibroid with advancing pregnancy at times seems unbelievable. During labor one must be on the lookout for the following complications.

(1) Impaction of the tumor in the pelvis before the fetal head.

(2) Uterine inertia.

(3) Ruptured uterus due to abnormal presentation or weakened wall after myomectomy.

(4) Tumor necrosis or twisted pedicle.

In those cases necessitating cesarean section, the decision to choose between myomectomy or hysterectomy depends on the size and situation of the tumor, ease with which it can be removed, condition of patient at the time of operation, age and parity. In a young woman every effort should be made to conserve the procreative powers.

The following case presents many interesting angles in the conservative treatment of a patient with fibroids.

Mrs. P. L. D., aged 33, had myomectomies in 1924 and again in 1926, one of these being a large pedunculated submucous fibroid which almost filled the vagina. Six years later, the patient had a normal pregnancy with a large fibroid the size of an orange on the anterior wall, which caused no symptoms. On October 24, 1932, labor was induced by rupture of the membranes and after six hours of moderately severe pains, a male infant weighing 7½ pounds was delivered by low forceps. The puerperium was uneventful and afebrile.

The patient was readmitted to Memorial Hospital on September 10, 1936, with a diagnosis of pregnancy at term and multiple myomata uteri. After two hours of labor, examination revealed that a large fibroid had slipped into the pelvis in front of the fetal head. The cervix was not effaced nor dilated. Cesarean section with hysterectomy was done and a normal live male child, weighing 7 lbs. 1 oz., was delivered. Recovery was uneventful.

OVARIAN TUMORS

Ovarian tumors are much more frequently the cause of sterility than fibroids, because of the likelihood of destruction of the entire ovary. Dermoids and chocolate cysts are frequently bilateral. Pregnancy, however, is not complicated by ovarian tumors as frequently as by fibroids. Lynch found the incidence of ovarian cyst at the University of California Hospital to be 1 in 1,500, while at Sloane Hospital it was 1 in 500. In our series there were only 7 cases of ovarian tumors associated with pregnancy, or 1 in 650. One cyst had to be removed at four months because of a twisted pedicle and the pregnancy continued thereafter without interruption. In two cases, the cysts were removed at delivery by cesarean section because of their enormous size; one obstructed labor and necessitated cesarean section with its removal. Only one case caused any complication during the puerperium. This was a single cyst which became infected six weeks after delivery. After a stormy convalescence an abscess formed in the *cul-de-sac*. With drainage of the abscess,

the entire degenerated cyst wall was passed through the posterior colpotomy incision. Following this the patient made an uneventful recovery. Two cases occurred in the early months of pregnancy which presented all the classical symptoms of ruptured tubal pregnancy: sudden knife-like abdominal pain with fainting, leukocytosis, rapid weak pulse, abdominal tenderness and rigidity. Aspiration of the *cul-de-sac* showed fresh blood. Laparotomy disclosed a ruptured corpus luteum cyst with a large amount of free blood in the peritoneal cavity. Unilateral oophorectomy in both cases controlled the hemorrhage. In one case pregnancy continued uneventfully until term, while in the other case the uterus was removed because of a severe nephritis with toxemia. In such cases it would be wise to use progesterone if the corpus luteum has been removed or injured. The safest period in which ovarian cysts may be removed is between the fourth and fifth month. All effort should be made to conserve the corpus luteum until placentation is complete or to use substitute endocrine therapy. McKerran says that the incidence of development of twisted pedicle in ovarian cyst is 8 per cent in nonpregnant, 12 per cent in pregnant, and 20 per cent in puerperium. With only 7 cases one cannot draw conclusions. Ovarian cyst may be a complicating factor during pregnancy, labor, or puerperium. The procedure in handling it has to be individualized and conservation of ovarian tissue whenever possible is strongly advocated. Cases of fatal peritonitis have been reported which were caused by the rupture of a dermoid cyst and the irritating effect of its contents. Aspiration of an ovarian cyst through the vagina, while strongly condemned by some gynecologists, has proven of special benefit in individual cases.

MISCELLANEOUS TUMORS

While extremely rare, pregnancy and labor have been complicated by bladder tumors as well as a misplaced kidney in the pelvis. In this small series there was a case of tumor which obstructed the pelvic canal, and after a mistaken diagnosis of myoma, cesarean section with hysterectomy revealed a broad ligament abscess containing about 500 c. c. of sterile pus. Convalescence was uneventful in this case although the patient had had an unsuccessful attempt at delivery by forceps before she was seen in consultation. Another case of a melanotic sarcoma which had its primary origin in a mole behind the right knee, metastasized so rapidly that the pelvis and inguinal region were filled with these metastatic growths, necessitating a cesarean section shortly before the date of expectancy. The patient died six weeks after delivery with metastasis throughout the entire body. The third case occurred in a primapara who was delivered at term by low cervical cesarean section because of pelvic dystocia. This patient had myelogenous leukemia during pregnancy and her sister had died the year before of the same disease. About ten days after delivery, a freely movable firm round mass about the size of an orange could be felt in the lower abdomen which was not closely associated with the uterus. The patient had slight elevation of temperature off and on for six weeks, and some abdominal pain. With consent of the family, an exploratory laparotomy was done under local anesthesia and revealed a fibroma involving the greater part of the wall of the transverse colon. There were no symptoms of obstruction caused by the tumor and due to the leukemia, no surgery was done. This patient, while still alive after two years, has all the symptoms of myelogenous leukemia.

SUMMARY

There were only 47 cases in approximately 4,500 deliveries in which tumors complicated pregnancy. Fibromyomata uteri accounted for at least three-fourths of these cases. The operative incidence in cases of myomata was high, as one would expect. The age of the patient was usually the middle thirties. Toxemia of pregnancy with hypertension and albuminuria was found in 40 per cent of cases with fibroids. The usual symptoms of antepartum bleeding, necrobiosis, postpartum hemorrhage, malposition of the fetus, retained placenta, and mechanical obstruction to labor were noted in this series. Cesarean section with hysterectomy seems to be a very wise procedure in a large number of cases. Myomectomy is indicated whenever the site of the tumor permits and the patient is in the early reproductive age. Ovarian and miscellaneous tumors may cause complications during pregnancy, labor and the puerperium in a very limited number of cases. Playing the law of probability, one should regard any sizeable tumor associated with pregnancy as a distinct threat to the patient's safety and extra precautionary safeguards should be employed.

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DISCUSSION (*Abstract*)

Dr. W. T. Pride, Memphis, Tenn.—Dr. Johnston has given a good resume of what occurs to a patient who is pregnant and who has a tumor. I do not think he mentioned specifically that this often occurs. We find fibroids early in pregnancy more often near the fundus. During pregnancy the growth is very rapid and at the time of delivery the tumor is sometimes as large as the baby's head. On two occasions I had not known that a fibroid at the fundus was present and after delivery of the baby thought another baby was there, because when I felt the uterus it felt just about as large as a baby's head. These fibroids do not cause any trouble and usually disappear later on.

I had occasion to operate upon one of these cases two or three years later. I wondered what became of the fibroid. I had the uterus in my hand and I could not find any sign of it. When the condition occurs in a young woman, as Dr. Johnston said, we want to give her a chance. A hysterectomy is to be avoided. We have done myomectomies upon a number of patients during early pregnancy. This is not desirable, as these cases sometimes bleed and adhesions follow the operation. If the fibroid is situated low in the cervix and we think there is no chance for the woman to deliver, of course, we never allow her to go into labor. We do a cesarean and hysterectomy, if necessary, without any ill results at all. Degeneration of the fibroid from pressure, as Dr. Johnston said, is one of the most serious complications we can possibly have, and the question comes up constantly whether the young woman with a fibroid situated fairly low should be operated upon early. This case is allowed to go as far as possible. If the patient presents any undue symptoms we operate upon her at that time.

With ovarian cysts, treatment depends entirely upon the cyst and the rapidity of growth. Sometimes these cases, as Dr. Johnston said, have a great deal of bleeding during pregnancy and the puerperium, and we have to operate to save the patients' lives. Then comes the question, if the patient is at about the fifth or sixth month and an operative procedure is necessary, leaving the uterus in place, what is going to happen to the patient if she goes into labor? Sometimes it is quite a problem to know whether we really should wind up the pregnancy then, or allow it to go on to term. Sometimes when the uterus is left a second operation is necessary.

I remember a puzzling case which Dr. Litzenberg saw with a physician near Memphis. Dr. Litzenberg had palpated the abdomen and outlined five fibroid tumors. He recommended that she go until about eight and one-half months, and then a cesarean be done and later a hysterectomy. I did the cesarean and the hysterectomy with very good results. With ordinary fibroid tumors it does not seem to be any trouble to do a hysterectomy at the time of the section.

I hope that we can sometime establish a routine procedure for these cases, because it is always a puzzle. Whether we should carry on the pregnancy and risk another pregnancy later on when the tumor has disappeared, because these tumors really will disappear in the interim, is a question.

Dr. Martin C. Hawkins, Jr., Searcy, Ark.—There are two types of tumor, namely, those that we interfere with and those that we let alone. If there is any doubt at all as to the procedure near term, cesarean section should be resorted to as a conservative measure.

Solid ovarian tumors, especially dermoid cysts, advance faster with the progress of pregnancy, and I believe that solid tumors of any appreciable size should be removed between the fourth and fifth months of pregnancy, provided there are no contraindications in so far as the patient herself is concerned.

Dr. Charles Edwin Galloway, Evanston, Ill.—I do not quite understand Dr. Johnston's incidence of dermoid cysts. About eight out of ten ovarian tumors, in the general run of cases complicating the first pregnancy, will be dermoid tumors of the ovary. It is a good idea to get an x-ray of the tumor first, because you may see calcium in it, and also the patient may even go on to term with a tumor of considerable size in an ovary.

If we are dealing with a fibroid of the uterus which is obstructing labor and we decide to do a cesarean section for one reason or another, cesarean section and myomectomy should not be done at the same time. It is safer to do a cesarean section, and if the myoma is large, or if there are multiple fibroids, it had better be hysterectomy following cesarean, but not a myomectomy following cesarean, because the bleeding associated with myomectomy at the time of cesarean has a very dangerous effect.

Dr. W. T. McConnell, Louisville, Ky.—The things that have given me the most grief are small, undiagnosed submucous fibroids that grow during pregnancy and are undetected. The bleeding in this type of tumor comes on late, sometimes after the patient has gone home from the hospital. It is often very profuse. After involution has occurred we can map out the submucous fibroids.

I do not believe this point was mentioned, but it has been the source of our greatest grief.

Dr. E. C. Hamblen, Durham, N. C.—I recall having seen, some 8 years ago, a quite rare type of tumor complicating a pregnancy of approximately 6 weeks' duration. It was a cyst of the uterus which measured some 13 cm. in diameter and which arose from the right lateral and posterior portion of the uterus (reported in the *American Journal of Obstetrics and Gynecology*, 31:530, 1936). Gross and histologic studies of this cyst led to the conclusion that it was of embryonal origin, from remnants of the Wolffian system. So much did the tumor simulate an ovarian cyst that the patient was demonstrated to the ward round group of students as having that condition. Operation was done presumably for an ovarian cyst. The pregnancy was not anticipated. No symptoms had been experienced except that of a mass in the lower abdomen. The patient had had five previous pregnancies, all of which were uncomplicated. It seems reasonable to assume that this cyst had been present for a number of years;

its recognition by the patient as a mass was probably due to its upward displacement by the pregnant uterus. The uterus, containing the cyst and pregnancy, was removed. While there was considerable thinning of the uterine wall at the point of origin of the cyst, it is conceivable that pregnancy might have continued without uterine rupture.

Dr. Johnston (closing).—Formerly I regarded any tumor complicating pregnancy as probably not destined to be troublesome. I thought it would not be difficult to deliver a patient with a tumor. When you review your cases or permit somebody else to review them, you will find that you have many more difficulties and many more complications than you thought you had.

Fibroids can simulate almost anything. One of our cases simulated a ruptured tubal pregnancy. We thought that we had made a diagnosis. Dr. Bertner saw this patient with me. The tumors were removed, and we learned that the symptoms were all due to degeneration and small fibroids. These tumors simulate placenta. They can cause trouble after delivery. When a tumor complicates pregnancy, whether it be fibroid, ovarian cyst, or what not, we should watch these petients most carefully, because, regardless of clinical impression, the law of probability is that the majority of cases will require operative interference, either at the time of labor or some time during the first six weeks of the puerperium.

Only two of our cases had dermoid cysts. Dr. Pride mentioned disappearence of tumors. I do not believe that I have had any instances of that kind. What causes fibroids? Are patients with fibroids poor surgical risks to begin with? Is there any associated cardiac condition, which has sometimes been spoken of?

In our experience with this limited number of cases, we have found that when they go into pregnancy or labor, they are most likely to require some operative interference, and we should safeguard their lives by taking all the precautionary measures possible.

RADICAL MASTOIDECTOMY*

By ERRETT PACE, M.D.
Paducah, Kentucky

Radical mastoidectomy was so termed by von Bergman in 1889 and improvements in its accomplishment have brought it to its present perfection. Its purpose is to remove from the middle ear and surrounding mastoid process all diseased tissue that may be potentially dangerous to the life of the patient. Since this is the case, we must divide our chronic otorrheas into the potentially dangerous and the non-dangerous groups before we can intelligently select the cases requiring surgery to the temporal bones. In the non-dangerous type the pathology is limited to the lining membrane of the tympanic cavity, and is the result of a chronic or recurring infection of this membrane never spreading to the surrounding bone. I mention this condition for the purpose of emphasizing the fallacy of operating upon a diseased ear of this type.

In the last few years there has been great improvement in the early treatment of ear infections. They are seen earlier by the otologist, and the drum membrane is incised at the proper time. Diagnostic acumen reveals the contributing causes earlier in the disease. Bacterial examination identifies the dangerous infections that are prone to develop complications. Constitutional conditions such as tuberculosis and lues that are contributing to chronicity are more readily recognized. We can see our patients more frequently and thus observe the progress of the disease to such an extent that radical operative procedures are not so frequently necessary as in previous years, and it is this advance in the treatment of chronic otitis media that I want to bring to your attention.

Let me state here that I am fully aware of those potentially fatal conditions and agree that nothing short of radical mastoid surgery is of any avail. Nevertheless, with our low mortality from radical surgery and living in an age when everyone wants quick results, we sometimes grow tired of conservative measures, and after seeing the patient too many times frequently decide on some radical procedure where as good or better results might be obtained by conservative measures.

Kopetzky[1] says:

> "The type of bony structure which the temporal bone presents predicts the kind of lesion which will develop when bacteria invade the middle ear spaces, the progress of the lesion and even the prognosis. The progress or regress of the lesion may be determined by roentgenograms and blood examinations, and bedside observations will denote the reaction of the patient to the disturbed physiologic function.
>
> "The temporal bone as a whole, including the middle ear, the mastoid process, the petrosal pyramid, the labyrinth with its venous network anastomosing through the temporal bone, and even the meninges which line its visceral side, must be considered in the study of middle ear infections."

We are all familiar with the patient who gives a history of a discharging ear for years or even decades, but assures us that his ear never bothers him except for a small amount of discharge and more or less loss of hearing. Careful examination will reveal that the only structures in-

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

volved are the mucous membrane of the eustachian tube and of the middle ear, the drum membrane and possibly the aditus and antrum. The typical drum findings are either the large central perforation without any destruction of the ossicles or a perforation in the anterior inferior quadrant which is said to be indicative of eustachian involvement. In this type the discharge is usually without odor due to the fact that there is no bony necrosis. However, copious secretions and decomposed exfoliated epithelium may produce an odor. This is a good diagnostic aid, since the odor disappears when the ear is cleaned completely by irrigation. The amount of hearing differs greatly in different cases. Some individuals seem to hear fairly well, especially for higher notes, while others have difficulty in hearing the spoken voice. In cases of prolonged suppuration there may be a mixed deafness probably due to a toxic effect on the cochlear nerve. Vestibular examination will be found negative.

We may not always find our patients with clear-cut and easily differentiated conditions, because the chronic ear can become dangerous at any time, and there may be borderline changes that make an exact interpretation almost impossible. However, these are usually not emergency cases and allow for time enough to make clinical observations and laboratory tests which suffice to give us an accurate picture.

Chronic otorrhea is most frequently found in those individuals who are neglected in the early stages of acute otitis media. Kopetzky[2] says that,

"In many cases the otologist can predict a long-protracted otorrhea by the discovery of a completely sclerotic mastoid on x-ray examination.

"When an acute otitis media occurs in the presence of a completely sclerotic mastoid process, one can be reasonably certain that an acute mastoiditis will not develop, and the patient should be prepared for a long-protracted otorrhea. * * * When, however, the suppuration of the tympanic mucosa is not accompanied by sclerotic bone, a typical acute mastoiditis will manifest itself when an acute infection supervenes on the existing chronic lesion. This lesion is commonly termed an 'acute exacerbation of a chronic mastoiditis,' but according to the pathologic findings such terminology is inaccurate. As has already been shown, the mastoid process is unaffected or is the seat of a secondary bone reaction, and since one cannot speak of an exacerbation of an infection where none has existed previously, the lesion must be considered as an acute mastoiditis. Once this idea is clearly understood, the necessity for the eradication of the lesion in the mastoid process becomes obvious. The symptoms of the middle ear suppuration continue after the removal of the mastoid infection, just as it would have if a mastoidal infection had not been superimposed on the chronic middle ear disease. A tympanomastoidectomy is not indicated for the lesion here described."

Children can often be relieved by general supportive treatment in the form of vitamins, proper diet, medication to the middle ear and in many cases the removal of infected tonsils and adenoids terminate a discharge that resists all our efforts to relieve by conservative measures. Sinusitis comes in this same group and should be given our best thought in all cases.

Graham[3] says:

"Children are a law unto themselves and will respond quickly if given a little help. An irritation such as a nasal or throat infection or constitutional condition such as lues or tuberculosis is readily communicated to the ear, and the ear trouble disappears readily under treatment of the mother condition. So thorough study of the individual is an essential, but often neglected, duty of the surgeon.

"In my early experience I had occasion to remove the adenoids and tonsils of some 50 children under the age of 14 who had been suffering for an indefinite number of months or years, with suppuration of the ears. In only one instance in these cases did I fail to obtain a cessation of the drainage and in this case I made a diagnosis of tuberculosis, later did a radical mastoid operation and procured a satisfactory result."

Unless there is immediate danger of loss of life those children of school age should be given the advantage of watchful waiting. They should be seen at frequent intervals for thorough inspection of the ear after cleansing. X-ray of the mastoid should be made to determine whether it is sclerotic. If it is sclerotic, a cholesteatomatous mass will not penetrate the hard bone and consequently be potentially more dangerous to the labyrinth, facial nerve, and surrounding structures than if the mastoid were pneumatized and offered little resistance to pressure. If seen early some ears can be cleansed and the exfoliated epithelium can be removed from the middle ear. Operation is postponed where there is deafness in the opposite ear. In this way one prolongs the child's period of normal education as much as possible. This same principle applies to old people who are not physically able to stand an operation.

In such cases every advantage of conservative treatment should be used and one should follow a course of watchful waiting as long as is consistent with safety.

CONCLUSIONS

(1) Not all chronic running ears are candidates for a radical mastoid operation.

(2) Children are a rule unto themselves.

(3) Chronic ears in children are frequently relieved by adenoidectomy and tonsillectomy with general supportive treatment.

(4) Proper care in early acute otitis media prevents many ears from becoming chronic.

(5) All chronic ears except those offering an immediate threat to the life of the patient should be given conservative treatment before surgery is decided upon.

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DISCUSSION (*Abstract*)

Dr. Louis Daily, Houston, Tex.—The radical mastoid operation is one operation that is not done often enough. Patients with chronic discharging ears are usually treated and carried along for years; many develop serious complication that could have been avoided by an early operation.

I shall recite in short the progress of two cases out of a series. Last year, I operated upon a white boy, age eleven. His only symptom was a profuse foul discharge from the ear since childhood. I found a perisinus abscess and extensive bony destruction about the antrum. The middle fossa was exposed but the dura looked normal. He made an uneventful recovery and left the hospital in 10 days. The ear epidermized in 10 weeks. One year later he suddenly developed severe headache, expulsive vomiting, coma and died in a few days. Autopsy revealed a large temporal lobe abscess. The pathologist reported on the microscopic examination that the abscess was of long standing and that it had become sterile. Evidently it was present at the time of the operation and only when it became large did it cause symptoms. His mother refused operation a few years before.

A young man, age fifteen, had had a discharging ear since he was 3 years of age, following measles. He had spells of nausea and vomiting, dizziness, and headache on and off. He was advised to have an operation when he was 8 years old, during a severe attack. It was refused and he was treated in the usual way. When I first saw him in the outdoor clinic he was very dizzy, and had severe headache and a high temperature. I operated upon him the same day and found extensive destruction of the mastoid bone and a lateral sinus thrombosis. He died 14 hours later. Autopsy revealed mural clots down to the innominate vein, infarcts in the lungs, spleen and endocarditis. An early radical operation would have prevented the fatal complications in both of these cases.

For years I have urged a radical mastoid operation in all cases where the patient gives a history of spells of unilateral headache, dizziness, nausea, no matter how infrequent these spells may be. Our results with the radical mastoid operation have been as good in children as in adults. Usually we get a dry ear in a few weeks, and a complete epidermization in from six to twelve weeks.

Your successes will depend on how thorough your operation is and upon the technic of your operation. In a small percentage of our cases a discharge, more or less, from the eustachian tube continued. We must bear in mind that we do not operate for the discharge nor to improve hearing, but to save life. Dr. Lempert claims that the discharge from the tube often is caused by sloughing of the tensor tympani muscle. In his course he teaches how to remove the muscle with its long root. Since returning from New York I have done it on the living in two cases.

Dr. Pace (closing).—I hope I did not leave the impression that I do not do radical mastoids. I always try to divide my cases into the dangerous and the non-dangerous, and I agree that in any intracranial complication certainly there is an indication for radical mastoid surgery.

PEPTIC ULCER*

A RESUME OF OBSERVATION AND STUDY

By LAY MARTIN, M.D.
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INTRODUCTION

When I began to think of topics which I felt competent to present to you with any degree of that assurance and authority which you have reason to expect of your Chairman, it seemed that the subject of peptic ulcer approximated my ideals for the fulfillment of such a presentation. If the discussion seems incomplete, it must be, for the subject is too large; and if it seems one-sided, it may be, for I wish to relate to you what I know about it from the approach of observation and study, rather than from an historical background.

PATHOLOGY

From a large mass of data, some accurate, some theoretical, it seems wise to lay before you, in the simplest manner, some of the fundamentals that we actually know about the subject. Peptic ulcers occur in the stomach and the duodenum. Those on the gastric side of the pylorus occur most frequently in a limited area of the lesser curvature. Those in the duodenum are scattered over the small area of that portion of the intestine. They may occur singly or in multiple. They may involve one or more of the coats of the gastro-intestinal wall. At times they are surrounded by areas of gastritis; at other times they are clean cut. They are seen

*Chairman's Address, Section on Gastroenterology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

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far more frequently in the duodenum than in the stomach, and more frequently in males than in females.

Complicating the ulcers are hemorrhages which may be large or which can be determined only by the estimation of occult blood in the stool. Another complication which we recognize is perforation. Experience and observation have taught us that ulcers can and do heal and, at times, leave no scar. At other times, scar tissue formation remains and becomes a secondary factor of considerable importance in the diagnosis and treatment of the condition. These facts may be called direct knowledge from a number of fields of investigation.

DIAGNOSIS

From other sources, as clinical symptoms, x-rays, gastroscopy, analysis of gastric secretion, we have learned other manifestations and results of the disease.

(1) Since the institution of x-ray photography and fluoroscopy as a routine procedure in the diagnosis of ulcers, we have learned to recognize certain changes in the normal pattern as pathognomonic of ulcer. In the stomach it is commonly observed as a niche on the lesser curvature; however, different patterns may be noted in the anterior and posterior walls, in the cardiac portion, and at times, in the greater curvature. We have learned to recognize certain changes in the pattern of the duodenum as caused by ulcer. Some investigators, in their enthusiasm, claim they can recognize certain very early changes which, to the more conservative of us, are not yet sufficiently understood to be of diagnostic significance. The gastric ulcer niche frequently disappears from the stomach and changes which we interpret as healing take place in the duodenum. These phenomena usually parallel clinical improvement or cure. Certainly, between attacks, the patients present no clinical evidence that the stomach or duodenum is handicapped.

(2) Abundant data have shown us that peptic ulcers are almost invariably associated with an hypersecretion of gastric juice and an increase in the normal titratable acidity of the gastric juice. This hypersecretion is also accompanied by an out-pouring of pepsin.

(3) For years we have been able to recognize a symptom-complex which, in itself, is almost pathognomonic of peptic ulcer. Epigastric pain, relieved by food, and returning as the stomach empties itself is a complaint known to you all. The hunger pains disappear as the ulcer activity abates and healing sets in. In the classical ulcer syndrome, symptoms appear at regular intervals during the year, for example in the spring and fall. Changes that are produced in this periodicity are frequently the result of cicatricial tissue formation which narrows the pyloric opening and leads to gastric retention. This leads to symptoms which differ from the typical pattern and which are, at times, difficult to classify.

(4) On physical examination we have learned that it is very difficult to demonstrate any actual changes that indicate an underlying ulcer. I have learned to recognize that individuals who have a single tender point situated somewhere along the epigastric line frequently have a peptic ulcer, even though their histories may not be of the classical type. Frequently one finds a small epigastric hernia as the cause of the area of local tenderness, and often associated with symptoms suggestive of ulcers. As a further complication, we not infrequently find epigastric hernias and peptic ulcers occurring at the same time.

As one sees more and more patients with duodenal ulcers, it becomes evident to the interested observer that a large number of these sufferers have physical and mental characteristics which are suggestive of an ulcer tendency. Many of the patients are high-strung, tense, supersensitive individuals who react badly to conditions of life which seem to them rigorous and difficult, conditions which, by the average person, can be weathered and readily withstood. I do not mean to infer that this constitutional characteristic is always found, but there is no doubt that ulcers are more prone to occur in this type of individual than in the more phlegmatic type.

(5) By means of gastroscopy, ulcers have been seen and healing noted.

ETIOLOGY

These data, not particularly numerous and certainly not difficult to understand, have, with the exception of the facts gleaned from x-ray and gastroscopy, been in our hands since early in the previous century. It is but natural that they should immediately suggest problems to a number of individuals. The first thought that would probably occur to one is, "What causes the ulcer?" Of the other questions which would have suggested themselves, some are reasonably well answered; others plague us today. What

causes the pain? Why the periodicity of attacks? What causes the hypersecretion of gastric juice? What relation has the psychobiological make-up of the individual to do with the development of ulcer?

In the effort to try to answer the first and most logical question, "What causes the ulcer?", a number of men have advanced ideas and thoughts culled from investigation. I do not wish to go into the background of the numerous theories that have been proposed, for that is not in keeping with the nature of this address. The main conceptions of the various etiological agents may be expressed as follows:

(1) Vascular changes in blood vessels supplying the affected parts.

(2) Changes in nerves supplying the affected parts.

(3) Focal infections, prominently studied by Rosenow, from which particularly selected bacteria were stated to lodge in the duodenum and cause an ulcer. This theory gained a number of adherents and for years teeth, tonsils, adenoids, and other alleged foci of infection were removed without notable demonstration that significant numbers of ulcers were being healed.

(4) Endocrinopathies.

(5) Vitamin deficiencies.

(6) Gastritis has been suggested as the sole or contributing cause. As yet, no noteworthy data have been published to substantiate the ideas of the respective proponents.

(7) Allergy is an attractive idea. Many factors suggest themselves, such as seasonal periodicity of outbreak, the likelihood that healing sets in under the stimulus of nonspecific protein therapy. These are ideas not altogether unsubstantiated by observation and experiment, but it must be recognized that the idea has not, by any means, been proved.

(8) From the early days, it was noticed that an hypersecretion of acid gastric juice was almost inevitably found in association with peptic ulcer. One should not wonder that many physicians saw etiological association between the two. Today there are many who believe the ulcers are produced by hyperacidity and increased proteolytic activity. As yet, no adequate proof has been forthcoming.

(9) The psychogenic basis of peptic ulcer is a possibility that will bear close scrutiny. More and more it has been recognized that ulcers are particularly likely to occur in high-strung, tense, easily disturbed individuals.

As you see, the various theories try not only to suggest the cause of ulcer, but also are related to one or more of the various conditions that accompany it. No incontrovertible or convincingly plausible evidence has been adduced in support of any of them.

TREATMENT

When we summarize what we know about treatment, we realize that for years peptic ulcer patients have been subjected to a discouraging number of forms of therapy. As we look back upon some of them, it cannot be with pride, for they are little short of absurd and have been generally recognized as such.

A few helpful agents have, however, been noted and are as follows:

(1) *Rest.*—It is not always necessary to enforce this in the early or mild cases, but in the more advanced cases it is an invaluable aid.

(2) *Bland Diet.*—There is abundant evidence that when sufferers from peptic ulcers use bland foods they are much more comfortable throughout the day than when general or coarse foods are eaten. Many patients have noted that this form of dietary restriction, with the addition of intermediate nourishment, is frequently enough to keep them comfortable.

(3) *Neutralization of Gastric Juice and Medication.*

(a) *Alkalinization.*—There is adequate evidence that certain forms of alkalinization are, at times, helpful for the relief of symptoms.

(b) *Antispasmodics.*—In most cases of peptic ulcer, there is a notable hyperperistalsis of the stomach and a pylorospasm. Significant data warrant the expectation that adequate doses of belladonna or its derivatives will lessen the hyperperistalsis and pylorospasm. In the hands of many clinicians, this has been a most satisfactory drug for the alleviation of symptoms.

Other similar agents have been suggested which, from usage, have not yet convinced us as being superior. Trasentin is now in vogue, but it is too early to do more than speculate about its place in the therapy of ulcer.

(c) *Miscellaneous.*—Nonspecific protein therapy has a field of usefulness. Some years ago, parenteral injections of various proteins were used abroad, especially in Germany. Later on, they were utilized in this country.

DISCUSSION

With this summary of the facts about peptic ulcer, its pathology, complications, signs, symptoms, gastric juice and x-ray findings, with an outline of the various theories related to its etiology, and with a resume of the few principles of treatment which have been shown to be reliable and well founded, we may profitably enter into a discussion of some of the aspects of etiology and treatment.

In spite of our lack of exact knowledge of the etiology of the disease and our need for a specific remedial agent, it is possible for students of the condition to be impressed with certain phases of the disease and the influence of various types of treatment. It is these impressions and observations that I wish to present to you.

In its simple form, peptic ulcer is a self-limited disease that runs for a limited space of time and the patient returns to a normal state of health. The attack may return in a few weeks or months and the well-known, seasonal periodicity may set in. On the other hand, there may be no later recurrence; or it may recur years later. This is true whether the patient receives no, little, or what is accepted as adequate medical treatment. An evaluation of this simple, often-repeated cycle must needs give us pause when we try to evaluate various forms of therapy.

For years, we have, at the Johns Hopkins Hospital, been utilizing ambulatory treatment for the majority of the outpatients. It has been noted that when they are placed on a full bland diet of five or six feedings, with the addition of tincture of belladonna to tolerance, and some form of alkaline powders, a large number of them do very well. They continue with their occupations and, in time, if there has been positive occult blood in the stools, we find it becomes negative. Concomitant with the abatement of clinical signs, there are fewer indirect x-ray signs of gastric hyperperistalsis and irritability and, at times, we note changes in the ulcer area, which we believe are indicative of healing. So efficacious has this treatment proven to be that, in a large number of instances, our private patients are handled in exactly the same way.

It has been suggested that if all ulcer patients should be put at rest at home, or hospitalized, for several weeks during the acute stages of the disease, the period of activity would be diminished. This seems a reasonable thought. One has, however, to weigh the theoretical value of this enforced rest and loss of time against the fact that a large number of patients react quite well to ambulatory treatment and are spared the financial burden imposed upon them by loss of work, or the greater expense of hospitalization. Some physicians feel that if these patients are kept at rest during a period of activity, they are less prone to a recurrence. I have no figures to combat this belief, but when one considers the number of variables in each individual that have to be reckoned with in estimating the value of one or the other form of therapy, such a proposal seems to me untenable.

There are, naturally, a number of patients who have too much pain and discomfort to continue work. They are generally tired and frequently overwrought; they need rest and they receive it, either at home or in the hospital. In the majority of instances, they receive the same dietary and medical treatment as the more benign group.

At this point it might be well to say a few words about the dietary treatment of Muelengrocht. The conditions that have brought it preeminently to the fore are those that are concerned with the treatment of bleeding ulcer. For years we have been treating the patient who shows occult blood by the dietary regimen outlined above. It was the suggestion of Muelengrocht that we at once feed patients who had had a severe hemorrhage. He suggested the same diet that we have utilized as a bland diet, plus the addition of scraped beef and puree of green vegetables. He states that his mortality is as low as anyone's and that his patients recover sooner. It is, as yet, too early to evaluate the efforts of his treatment when utilized by a large number of physicians, but at present, I prefer to leave the patient rather quiet for a day or two and then start him off on a dietary regimen of small portions. He implies that most doctors have starved patients for days after hemorrhages and makes it appear that, in contrast, his idea of immediate feeding is a much more sensible arrangement. And indeed it would be, if most doctors did as he suggests. I do not believe that he is correct in that assumption.

These simple forms of therapy are usually effective in obtaining satisfactory clinical improvement and, at times, are apparently curative. Nevertheless, there are instances in which the results are disappointing or ineffective. When such conditions exist, one naturally searches

for other forms of therapy, at first, medical, and then, if necessary, surgical.

In the attempt to formulate other forms of therapy, one naturally tries to reach and combat the etiologic agent. As this is unknown, the obvious attack is along the paths suggested by the various theories on the subject. Those we shall consider deal with the potential hyperacidic, allergic, and psychogenic origins of ulcers.

As noted above, hyperacidity is almost invariably associated with peptic ulcers, and abundant experience has taught us that the patient feels better when the gastric acidity is partially or completely neutralized. This is a fact. A number of clinicians have felt that the persistence of symptoms is due to incomplete neutralization of the gastric acidity and that the proper form of treatment was one that aimed at complete neutralization as the great desideratum. They feel that unless this is obtained, one has not given the patient adequate treatment, and that an ulcer will heal much more quickly when the gastric juice is neutralized twenty-four hours a day. This is a theory.

The bad results obtained by overdosage of sodium bicarbonate, with the resultant alkalosis, are well known to you all. This undesirable condition enforced a marked reduction in the dosage of the bicarbonates and increased the usage of insoluble salts, such as calcium carbonate, bismuth nitrate, and barium sulphate, which no doubt was of value.

Recently the English have shown the advantages of magnesium trisilicate which buffers a large quantity of hydrochloric acid. More recently aluminum hydroxide has become recognized as of notable value in reducing symptoms. It is presumably the most satisfactory antacid we have. Perhaps time will show that it has some further properties than that of neutralization. So effective has it been that this should be considered.

In the effort to keep the titratable acidity at a low level, large amounts of these various neutralizing and absorbing chemicals have been given at frequent intervals. Many observers advocate methods of administration which will keep the gastric juice neutralized not only in the waking hours but also in the hours which should be allotted to sleeping. To this end, the so-called drip method has been introduced: A retention catheter is kept in the stomach day and night for varying periods of time. Through it measured amounts of milk or aluminum hydroxide are constantly introduced into the stomach. There may be instances in which this form of therapy is of value. There may be instances in which a certain proportion of patients has been relieved of symptoms earlier and the gastric ulcers, freed from the digestive juice of the stomach, have been healed sooner. It may be indicated and of value in the treatment of certain carefully chosen cases. I do not know, for I have never felt the need or occasion for its use. It should not, however, be used in the routine treatment of peptic ulcers. Most of them heal by themselves or under the simple, time-tested methods of treatment noted above. Those less sick patients are not confined to the hospital with the associated loss of time and expenditure of money; and what is more important, they are spared the ordeal of a complicated method and their future is not disturbed by the thought that a recurrence would indicate another such hospital experience.

It is yet to be demonstrated that neutralization of gastric contents is of fundamental importance in aiding the healing of peptic ulcers. It is reasonable to theorize that activated pepsin will retard the healing of a gastric ulcer and will slow up clot formation over a bleeding ulcer. It is another matter to prove it. The ulcers in the duodenum, contrary to those of the stomach, are bathed in a fluid which is proteolytically active when alkaline. If the gastric secretions are neutralized, one may reduce their potential digestive activity upon duodenal ulcers, but to the same degree increase their chance of being digested by the duodenal and pancreatic juices. Again, there is no direct proof that activated trypsin and erepsin will do this.

Since peptic ulcers are commonly found associated with gastric secretion of high titratable acidity, and since they are practically unknown in cases of achlorhydria, it takes but a small step to aver that hydrochloric acid is in some way responsible for the formation of peptic ulcers. There are a number of clinicians who hold this to be a self-evident fact.

At the present time, many of the proponents of this belief make a great point of the fact that jejunal ulcers have occurred in almost 100 per cent of the dogs which have been subjected to a type of gastro-jejunostomy (Mann-Williamson technic). In these animals, unneutralized acid gastric juice flows into their jejunums. When care is taken to keep the gastric juice neutralized either by technical methods which allow normal pancreatic secretion to pass over

the field operated upon, or by the introduction of alkalies, the incidence of jejunal ulcer is much less.

It is important to realize that we are not talking of jejunal ulcers in dogs which have been subjected to an unphysiologic operation, but of peptic ulcers in man, ulcers which occur in areas normally bathed in acid gastric juice, ulcers which appear and disappear when subjected to digestive juices of the stomach and duodenum.

It may be true that a stomach must be able to secrete hydrochloric acid before a peptic ulcer can form. However, that which we should like to know is what causes the primary lesion, be it erosion, or wheal, or area of inflammation upon which pepsin might act to produce an ulcer. There are innumerable individuals with gastric hypersecretion who do not develop an ulcer and, in truth, we do not really know that enzymatic activity is necessary to convert a postulated primary lesion into a fully developed ulcer. It seems plausible, but it has yet to be proven.

So far as we know from the results of gastroscopic examinations, small erosions may occur over the body of the stomach, but gastric ulcers are most frequently found along the midline of the lesser curvature. It seems very difficult to particularize ulcer formation from digestive action on only those erosions which, by chance, occur in a limited area. But whatever may be the etiologic influence of hypersecretion, there is no doubt that the patient generally feels better when the gastric juice is partially or completely influenced.

Some years ago we noticed that parenteral injections of a nonspecific protein produced relief of pain in patients with peptic ulcer in a relatively short time. This was an important observation, because it was noted in a large number of patients who had been on some form of medical regimen for months and without avail. It seemed, at first, that this might be a much sought-after cure, but the patients began to return with recurrences. However, so definite were the immediate effects that we were led to believe that the ulcers in a certain number of individuals might be allergic responses and that the results we were obtaining were those of nonspecific desensitization. Another circumstance which strengthened the tenability of this hypothesis was the recognition of the periodicity of the recurrence in many individuals, suggesting a seasonal character. This led to animal experiments which tended to support the idea. The problem is still unsolved and much work still awaits those interested. However, if certain ulcers are the result of allergic reactions, the obvious treatment is desensitization and removal of the patient from contact with the antigen. Although we do not understand the method of its action, it should be recognized that the effects of nonspecific protein therapy are, at times, brilliant. Therefore, it would be well to keep it in mind for usage on a purely empiric basis when the simpler forms of therapy are unavailing or when we might wish to supplement them.

In recent years medical attention has been more and more directed not only to the psychogenic basis of symptoms, but to a very probable psychogenic stimulus as the basis of certain demonstrable organic pathologic changes. Such conditions, as end results of essential hypertension, ulcerative colitis, possibly hyperthyroidism, and, most importantly, peptic ulcer, suggest themselves.

For a number of years I have been interested in the functional disorders of a gastro-intestinal character that unquestionably accompany various anxiety or psychoneurotic states. It needs but a cursory consideration of the psychobiological constitution of a large number of sufferers from peptic ulcer to realize that, as a group, they are more easily influenced by the adverse strains and stresses of life than the majority of persons who do not so suffer. The idea is certainly not only mine; it has been noted by a number of clinicians, and that number is increasing. It is an idea, however, which personal observation has convinced me to be sound and of fundamental importance; important not only etiologically, but therapeutically. Although it may not constitute the etiological basis as a unity, it is an integral part of the reaction which contributes to the establishment of the completed lesion.

You will recall that listed under known beneficial therapeutic aids was rest. Rest, physical rest, is essential, at times, because so many of these patients have been doing too much and, more important, doing too much when driven to it by a state of nervous tension. Rest in surroundings which promote peace of mind is of paramount aid, and this peace of mind can be obtained only when the patient lives in harmony with his environment. The frustrations and anxiety states which upset the patient's vegetative nervous system can be eliminated only when the patient has insight into and understanding of the various environmental conditions which up-

set him or which cause him to lead a life of increased nervous tension. There seems to be little doubt but that one or more of these causes of psychic unrest can and do institute a chain of reactions in the body which lead to the development of peptic ulcers.

Here, it seems to me, we were getting at the root of the matter. Treatments, such as alkalinization, repeated small feedings and alkalinization, bland diet with and without antispasmodics or alkalies, the tube feeding of years ago, the tube drip method of today, nonspecific protein therapy (Larostatine, the treatment which lasts practically the full length of the disease), either individually or in combination are accompanied by good clinical results; if one method will not work in the hands of one physician, in the hands of another it may. There you have it, the "laying on of hands," the faith on the part of the patient that he has found the doctor who will cure him. For a doctor to inspire such faith, is a tribute to his personality; for him to be able to relieve the patient, is a fine accomplishment; but for him to use complicated, unnecessary and expensive procedures to accomplish that result, that is decidedly not a tribute.

Since these patients can be treated by so many ways, since faith in the doctor or in the doctor's method is so important, it would seem that the patient's outlook, his state of mind, his psychic reaction to his environment, were important factors in the disease. It is encumbent upon the doctor not only to utilize his influence in the treatment of the immediate attack, but to educate the patient, to teach him the importance of psychogenic influences in their relation to the onset of symptoms and, as it seems, of organic changes.

The duodenal ulcer patient should be fully instructed in the nature of his ailment. He should be taught that ulcers tend to recur, and that nervous tension has a great deal to do with producing recurrence; that it is essential for him to live within his nervous limits. He must be taught to regulate his life, to learn that the important factor is not the activities in which he partakes, but the manner in which he partakes of them. It is not so much what he eats as his digestive state, as influenced by his psychic state, when he eats. Many of these patients suffer from anxiety states that may result from a number of conditions of life, of which overwork is only one. Worry over finances or family, domestic incompatibilities, types of occupation which are unsuitable, inability to see anything concrete in the future, lack of security, are but a few of the conditions which serve as the background from which the ulcer draws its origin. Only so much pressure can these patients withstand; beyond this they react in a series of phenomena which lead to the development of a peptic ulcer.

Utilizing to the best of our ability these various forms of therapy, diet, rest, psychotherapy, neutralization of gastric acidity, parenteral injections of nonspecific protein, the counsel of patients, the philosophy of accepting the ills you suffer rather than chance the uncertainty and dangers of surgery, we find on our hands a certain proportion of patients in whom surgery is indicated and justified. There are a few outstanding conditions and complications which point toward this form of therapy: perforation, intractable pain, continued recurrence of attacks, repeated severe hemorrhages, especially in middle age or beyond, food allergies which preclude the establishment of a bland diet, financial status of the patient which will not permit repeated absence from work, an unstable nervous system which will not respond to psychotherapy and is associated with repeated attacks, are some of the indications.

The idea has been circulated that surgery in the presence of a bleeding peptic ulcer is dangerous and contraindicated. There is no question that this belief is fundamentally sound if the patient is in a state of shock. This condition will ensue, at times, if operation is delayed too long. There is no sound reason why a patient who is bleeding should not be operated upon at that time, if his general condition is deemed capable of withstanding the strain of surgery. It is often the safest procedure, and if the patient ought to be operated upon later, it lessens the time of recuperation. It permits removal of the bleeding vessel and the diseased area, provided it is surgically possible, and it is fair to say that surgery which aims to remove the diseased area is the only type which should be projected and, if possible, completed.

SUMMARY

I have endeavored to present to you, in as concise and succinct form as possible, some of the aspects which to me seem of interest and importance in understanding and treating the patient suffering from peptic ulcer. This implies a consideration of the host and the peptic ulcer for, preeminently in this association, much of

the progress of the ailment depends upon the psychic status of the patient.

It is not too much to hope that the day will come when we shall regard peptic ulcer as a disease whose treatment is medical; when we shall look upon the patient who requires surgery not as one who has failed to respond to medical treatment, but as one who has not received adequate, sympathetic, and understanding attention.

PHYSIOLOGIC FACTORS AFFECTING BLOOD PRESSURE*

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Without a clear understanding of the extent to which blood pressure may vary from normal as the result of influences that are entirely physiologic, a determination of the amount of pressure resulting from disease would be extremely difficult.

The figures given in *Chart 1* are derived from a study of approximately seventeen hundred patients with normal and abnormal pressures.

The diagram shows the average rise and fall in blood pressure resulting from the effect of (1) a meal; (2) recumbency; (3) food plus recumbency; (4) vasoconstriction and muscle effort; (5) vasodilatation.

The normal pressure of a male 50 years of age is used.

Diagram 1 shows the average rise in pressure immediately following a meal. The level is maintained during the first hour; then the pressure gradually falls and by the end of the second hour returns to its original level.

Diagram 2 shows the average rise in pressure in the brachials when recumbent over that of sitting erect. Although this increase in pressure averages only 10 mm., it has been of considerable help in solving the cause of morning headaches, complained of by patients with hypertension, and the improvement or complete cessation of these headaches after the patient has been out of bed an hour or so. There is, apparently, a proportionate increase in pressure to the brain when the patient is sleeping, resulting in the severe headaches frequently complained of.

*Received for publication March 9, 1940.
*From the Medical Service of Norfolk General Hospital.

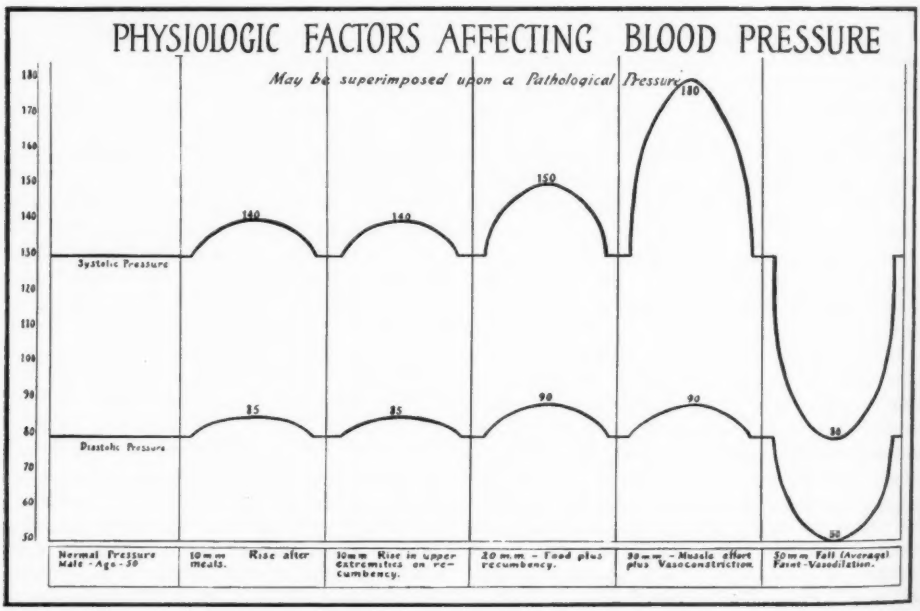

Chart 1

This type of headache is usually confined to the occipital region, but as the disease progresses the entire cranium may be involved. Considerable relief may be obtained by having the patient sleep with the head elevated upon two or more pillows until the pressure improves to a level below that in which the headaches occur.

Diagram 3 shows the average rise of 20 mm. that occurs when the patient is permitted to lie down after a meal may play an important role in a cerebral hemorrhage. This increase in pressure, although small, superimposed upon a hypertension that is already taxing an arterial system to capacity, may be the deciding factor in a cerebral accident. Patients in whom the systolic pressure is over 170 should not be permitted to lie down within two hours after a meal. If they wish to rest, have them do so sitting erect in a chair.

The average of Diagram 4 was obtained by placing patients with hypertension of varying degrees in bed, recording the pressure while ambulatory on admission and at two-hour intervals for twenty-four hours. The average patient's pressure fell 50 mm. within twenty-four hours. If bromides and nitrites were used, or one of the many sedatives containing a vasodilator, the time required to obtain this 50 mm. decrease averaged twelve hours. Frequently as much as a 50 mm. fall in pressure was observed within twenty minutes after the first reading was taken, due to fear and excitement at the time of the first reading.

Observation was made of a series of healthy persons, with normal pressures, while in a state of excitement or following severe exercise. The fall in pressure after they became composed or were at complete rest also averaged 50 mm.

This physiologic increase is significant when superimposed upon a pathologic pressure. However, rest and sedatives affect only pressures of physiologic origin and the level at which the pressure stabilizes, if above normal, is the level of the pathologic pressure. Although this type of pressure is transient it requires little imagination to see the danger zone a patient with a moderate or advanced hypertension reaches when subjected to stress or strain. Treatment should be directed to the pathologic pressure. If this is reduced within normal limits, the normal

BLOOD PRESSURES in BLONDS, BRUNETTES and NEGROES

TYPES	GROUP 1 NO. CASES	Student Nurses AVERAGE WEIGHT	AVERAGE AGE	AVERAGE S.P.	AVERAGE D.P.	Per cent to Normal S.P.	Per cent to Normal D.P.
Blondes	50	121 lbs.	20 yrs.	112	68	-7	-12
Brunettes	50	123 lbs.	19 yrs.	120	76	Normal	Normal
	Normal Pressure for age All diets the same.			120	80		
	GROUP 2 Ward patients (White) O.-P.-D.						
Blondes	50		39.8	122	72	-5	-7
Brunettes	50		38.1	136	84	+7	Normal
	Normal Pressure for age Diets variable			128	80		
	GROUP 3 Ward O.-P.-D.						
Negro Women	50		38.9	169	112	+32	+40
	Normal Pressure for age Diet very poor, particulary in red meats.			128	80		

All patients Wasserman negative.

Chart 2

physiologic increase, which is difficult to control, will give little concern.

The last diagram, showing the 50 mm. fall in pressures resulting from vasodilatation, was determined by recording the pressures of twenty-five-patients who fainted during or immediately following the withdrawal of blood from a vein for laboratory examination. All of these patients' pressures had been recorded a few minutes previously during the regular physical examination. Blood pressure readings were taken at ten-minute intervals during the first hour and at thirty-minute intervals until the patient's pressure returned to normal. The pressure in twenty-three patients became normal within the first hour, while two required six and four hours, respectively, to return to their original level. In one hypertensive patient the pressure fell from 160/110 to 110/66; after one hour it rose to 140/96, but it required six hours to reach the original level of 160/110. The pressure in the second patient fell from 110/70 to 70/30, and required four hours to return to the original level.

Chart 2 shows the variation in pressures in persons of different types. It indicates that brunettes are more prone to hypertension than blondes, and negroes more subject than brunettes.

In the negro group the diet, which was very poor, particularly in red meats, appears to be a factor. In four of these women pressures were normal, but their diet was well-balanced and contained an abundance of red meats.

Group 1 was composed entirely of student nurses. As they all lived at the hospital, the diet was essentially the same and could not have been a factor.

Group 2 was observed in the outpatient department and in the wards. Close questioning of the patients individually, as to diet habits and occupation, gave little reason to attribute the difference in pressures to these sources.

In the author's experience, hypertension in blondes occurred in only 0.9 per cent of approximately twelve hundred hypertensive patients.

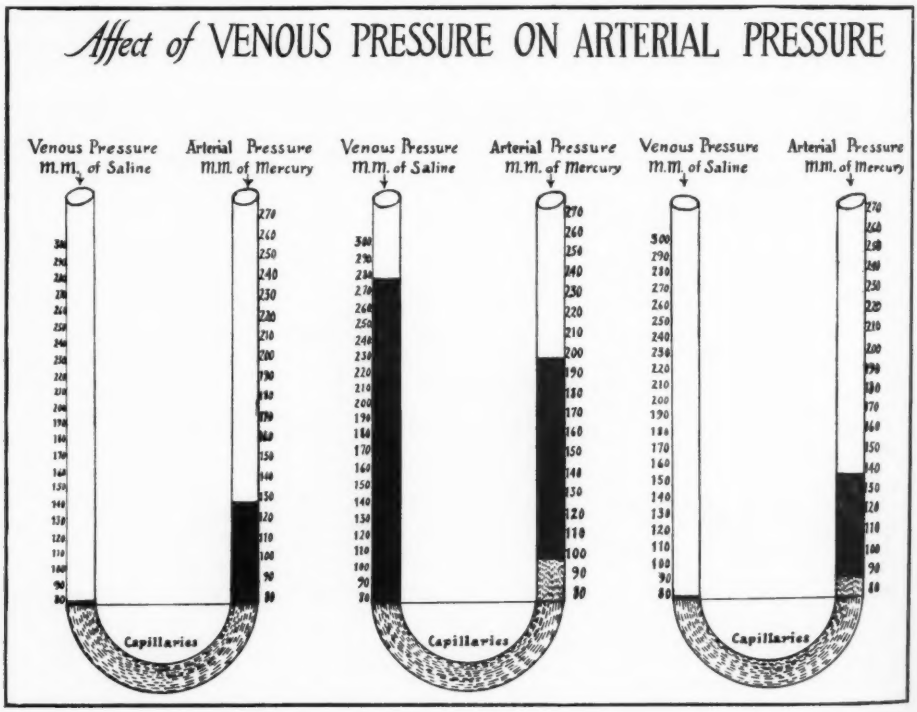
Affect of VENOUS PRESSURE ON ARTERIAL PRESSURE
Venous Pressure m.m. of Saline
Arterial Pressure m.m. of Mercury
Capillaries
Venous Pressure m.m. of Saline
Arterial Pressure m.m. of Mercury
Capillaries
Venous Pressure m.m. of Saline
Arterial Pressure m.m. of Mercury
Capillaries

Chart 3

At least two different readings were taken at intervals on each individual before the pressure was recorded. Particular care was taken to obtain the confidence of the negroes and in many cases the pressures were taken at intervals over a period of one hour before the final was recorded.

In *Chart 3* is shown the effect that an increase over normal limits in the venous pressure may have on the arterial pressure. The normals were determined by taking the venous pressures of forty males and thirty-five females whose ages varied from 20 to 50 years. Physical and laboratory examination showed these subjects to be normal healthy adults. Their pressures varied from 50 to 100 mm. of 0.9 per cent saline.

Elevation of the venous pressure may result from causes other than cardiac, but this communication will deal with those that are entirely of cardiac origin.

The effect of increased venous pressure, of cardiac origin, on the arterial blood pressure has not had much consideration in recent years. However, during the past four years, forty-three patients with abnormal venous pressures, associated with varying degrees in elevation of the arterial pressure, have been encountered. The response in the arterial pressure was in proportion to that obtained in the venous pressure.

In the first diagram the venous pressure is normal; also, the arterial pressure is in normal limits. The second diagram shows the effect that the increased venous pressure may have on the arterial pressure. Diagram 3 shows the fall

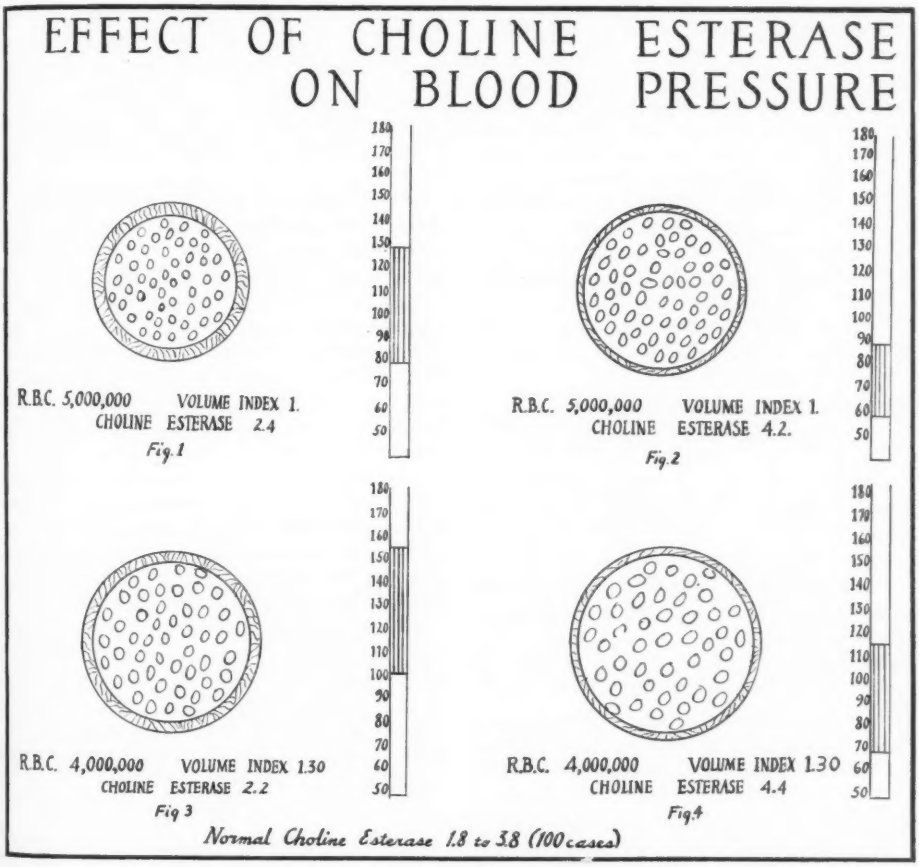

Chart 4

in arterial pressure after the venous pressure has been reduced to normal limits.

Hypertension resulting entirely from an elevated venous pressure will respond directly in proportion to the reduction of the venous pressure. Hypertension resulting from venous pressure and macrocytosis can be reduced in proportion to the reduction in the venous pressure and the reduction in size of the red blood cells. Where hypertension results from venous pressure, macrocytosis, and arteriosclerosis, improvement is equal to the reduction in the venous pressure and cell size only. The pressure will not return to normal, although the two first conditions may become normal, because there is a certain amount of pressure resulting from arteriosclerosis that cannot be improved. In hypertension resulting from venous pressure and arteriosclerosis, improvement in the hypertension will be only in proportion to that of the venous pressure.

Treatment should be directed entirely at the improvement of cardiac function. If this can be returned to normal through rest, sedatives, and digitalization, the venous pressure will in most cases improve proportionately. This will reflect on the arterial pressure, resulting in an improvement here. Venesection of these patients should be the last resort; because, as previously stated,[1 2 3] hypertension is usually associated with some degree of anemia and further loss of blood will in all probability impose a greater hardship upon the patient than the increase in venous and arterial pressure.

The effect of the choline esterase on the blood pressure will only be mentioned here, as a detailed report of one hundred cases will be published shortly. However, it may be stated that experiments indicate that hypertension does not occur if the choline esterase is above 4.*

In *Fig. 1, Chart 4,* the arterial tension is normal, the total blood volume is normal, and the cell size is in normal limits. The blood pressure is normal; choline esterase is 2.4. *Fig. 2, Chart 4,* is the same as *Fig. 1* except that the choline esterase is 4.2. The blood pressure is low: 90/60.

Fig. 3, Chart 4, shows the increase in pressure resulting from increase in cell size. The choline esterase is 2.2, indicating a normal vessel tonus.

Fig. 4, Chart 4, is the same as *Fig. 3,* but the choline esterase is 4.4, indicating a poor vessel tonus. The blood pressure is below the level expected from the volume index.

Investigation of the choline esterase shows that in patients with levels over 4, hypertension will not occur, although size and total number of red cells may be materially increased.

CONCLUSIONS

(1) The arterial blood pressure may vary as much as 50 mm. or more from the normal or the pathologic pressure as the result of influences that are entirely physiologic.

(2) Pressures that are well above normal on the first reading but return to normal within a few hours are the result of a physiologic variation and should not be considered pathologic.

(3) In pressure increases resulting from physiologic influences, the diastolic pressure lags considerably behind the systolic pressure.

(4) The level at which the pressure stabilizes above normal after all possible known physiologic influences are removed is the pathologic pressure.

(5) Pathologic pressures should be kept at their lowest possible level to prevent accidents which may occur from sudden increases due to a superimposed physiologic factor.

(6) Patients with hypertension, although the level may not exceed 200 mm., who fail to show any physiologic variations, have advanced arteriosclerosis and are in considerably more danger of some form of vascular insult than are those in whom the pressure is greater but who show these variations.

(7) Negroes are more subject to hypertension than brunettes, white persons and brunettes more subject than blondes.

(8) Abnormal elevations of the venous pressure may be reflected in the arterial pressure, producing an arterial hypertension.

(9) Hypertension does not appear to occur when the choline esterase reaches 4. However, no difference was observed in the level of the choline esterase in patients with normal pressure and in those with hypertension, indicating that in the former the vessel tonus is impaired, while in the latter it is normal.

*The figures used to denote esterase activity are the number of c. c. of 0.01 NNaOH required to maintain a pH 8 at 30° C. for a period of twenty minutes, using Congo-red as an indicator, a solution of 50 c. c. of distilled water CO^2-free containing 150 mg. of acetylcholine bromide and 0.5 c. c. of blood serum.[4]

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Driver Building

PROBLEMS OF A STATE MENTAL HOSPITAL*

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Tuscaloosa, Alabama

A discussion of the problems of a state mental hospital naturally involves a consideration of the proper function of this agency and its relation to the state government. As justification of a state's maintaining such a service, it may be said that one out of every five hundred of its citizens is constantly being maintained and treated there, and that within a period of the average span of life at the present rate, one out of every twenty-five persons now living can count upon admission to a mental institution at some time within his lifetime. When, in addition to this, we consider how seriously mental illness of a member of a family may affect or touch the lives and interests of other members of the same family, and further how mental illness and the behavior incident thereto may affect the interests of other citizens in a community, we begin to realize how close the welfare and conduct of a state mental hospital are to the general life and welfare of a community or a state.

This fact gives rise to what I consider the most important problem of state hospitals, namely, the political relationship to state government. So often it is reasoned that if a state maintains an institution, the state government, including its central official set-up, should have a close and immediate tie-up with it. Theoretically, according to current political science, a state hospital must be closely tied to the central state government through a bureau or central state welfare agency, in order that the institution may be controlled directly from the governor's office or the head of a state department, its board of control, superintendent, officers and general personnel serving at the pleasure of the governor or bureau. Such a close tie-up usually results in the administration of a state hospital's changing with each administration on an average of once every four years. Since the problems with which state hospitals deal require a long-time program, planned and mapped and projected well into the future, effective and efficient hospital administration cannot exist under this plan or is seriously handicapped, crippled and interfered with by constant and frequent interruption of management and administration. Since the mental hospital problems are peculiar to themselves and require specialization, both in administration and medical and nursing service, the legal set-up always should be one fully divorced from politics as politics operates in the average state. The governing body of state hospitals, which should include all state hospitals having to do with mental illness or mental deficiency in a given state, should be a non-political governing body, permitted to perpetuate itself by filling its vacancies itself, with gradual change of personnel, instead of any plan that would change its personnel by political appointment or otherwise totally and suddenly. Such a perpetual governing body insures the even tenor and even course of management, allowing and encouraging specialization, and therefore, permits and encourages, rather than prohibits, an institution or a group of associated institutions in the state making definite and positive long-time programs, fitting its program to the problems with which it must deal and projecting its programs far into the future. Wherever such a plan of government is not adopted by a state, it is found inevitably and unavoidably that special planning and pursuit of a rational program cannot exist because of frequent interruptions in management and interference from sources in no way familiar with the problems. To my mind this is problem number one with state hospitals the country over. Average, modern political science teaching sets up central bureaus under which such institutions may be directed or managed, entirely inconsistent with and incompatible with rational, effective, efficient and economical administration.

The problem of selection of personnel without a doubt ranks as problem number two in hospital administration, second only to the basic question of state set-up discussed in the foregoing paragraphs. The proper selection of staff and general personnel more than any other one thing insures success in hospital administration. Therefore, the method of selection of personnel to serve a state hospital must take into account certain self-evident truths and proven principles. It must, first of all, be recognized that

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*Read in Section on Neurology and Psychiatry, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

mental hospitals have a problem to deal with requiring a high degree of specialization of persons possessing by nature physical, mental, temperamental and moral equipment and capacity for specialized work. It must be borne in mind that only those by training and experience, conversant with the needs and necessary qualities of personality and character, can determine and rationally select personnel. Further, the harmonious relationship of employer and employee conducive to effective and efficient service in maintaining standards set up by the management must grant that management the privilege of selecting personnel to serve at the pleasure of the executive, under definite rules governing and regulating the service, either written or otherwise fully understood by both.

Without presuming to take any position either in favor of or opposed to the general principle of a Federal government, state, county or municipality's selecting its general employees by a civil service regulation, I am fully convinced that all officers, staff and other employees of a state hospital should be selected and serve under such regulations as may be set up by its controlling board and executive head. No agency could be expected to measure and determine this specialized service on a basis of merit so well as those already so specializing.

Unless the executive head of an institution is qualified either to select personnel or to set up the best method of selection of personnel, some other executive should be selected to replace him. All persons employed to work in any capacity in a state hospital should, first, be placed on probation, after tentatively qualifying to meet requirements, and only after a reasonable time for observing their qualities, physical, mental, temperamental and character, should they be placed regularly in the service. All nurses and attendants, particularly, should receive their training in the institution in which they serve. I doubt the propriety of the policy of employing persons who have received their training in other institutions.

Every individual in the organization, from the medical staff, superintendents of nurses, training school executives and nursing personnel down to orderlies and porters, should understand fully the program, plan, intention and major function of the institution in its responsibility to its patients and its attitude toward the public. Only this harmony of team work will create the proper atmosphere conducive to the best interest of its patients. Wherever mixed or cross purposes, disloyalty or lack of cooperation in the plan thus once understood is observed on the part of any officer or employee, the only remedy is his elimination.

I think I have in my long experience observed a tendency or trend for neurotic, and at times even psychotic predispositions, to seek employment with mental hospitals. For the good of the institution, as well as in the interest of the individual, persons constitutionally inclined or so predisposed by heredity should be discouraged or not employed, particularly on a medical or nursing staff of mental hospitals.

Lack of a general sympathetic understanding of the problem of mental disease and mental deficiency, and lack of understanding as to the important ramifications and relationships of this problem to the general welfare of a state and its people results in insufficient financial support as a rule. The average layman in public office, or in a state legislature, has no further conception of the problem than that it means a place to segregate, support and provide custodial care for a group of unfortunate citizens, who are to be hidden away from the public eye and forgotten by the rest of the race of mankind. Relatively few of the citizens of the state have any knowledge or impression of the great stream of humanity passing into and through mental hospitals and again out into life. The problem is such as not to attract public attention, and, therefore, its alumni, having no particular organization or political influence, cannot compete in lobbying for its share of the state's revenues along with those agencies constantly in the public eye, as education, good roads, public welfare and public health. Therefore, a program of acquainting the people with the problems with which state mental hospitals have to deal, their extent, magnitude and importance, in order to give them equal standing with other state problems, seems to offer a field for a certain type of publicity service. For this a volunteer, non-political and non-remunerated public citizens' committee has an opportunity of advising and informing the public and filling a gap which, of course, a medical organization, such as a mental hospital, has no disposition and no tendency to fill. This, it seems to me, ranks as problem number three.

After disposing of those problems that may have to do with the relationship of a public mental institution to the state and to the public and coming down to the closer problem, I would enumerate as problem number four the rather

retarded or retired specialty of psychiatry in its ranking with the other specialties of medicine in medical education. When we realize, as we should, that psychology is physiology, or that mental disease and mental deficiency are abnormal or disturbed physiology, we immediately place the study of psychiatry in the forefront of all subjects to be taught in medical school and to be properly understood and appreciated by graduates in medicine. We in the same manner of reasoning place psychiatry in the very dignified position of being, if not the most important specialty, among the most important specialties in medicine. Lack of proper understanding and proper appreciation of psychiatry as a branch of medicine in the past has permitted it to drift dangerously away from medicine toward the cults and metaphysics color, where disturbed functions and symptoms have been conjured with and dealt with as causes rather than merely expressions and effects. This would lead us, therefore, to insist upon a revamping of medical courses to include more extensive teaching and clinical experience and observation in psychiatry as a major problem affecting state mental hospitals.

The first conception of public institutions for mental illness had the single purpose of segregation and custodial care for the protection of society. This was crude and cruel, based as it was largely on superstition and fear, extending close down to us, as indicated in the witchcraft period of our own colonial days. Pinel slowly and gradually developed treatment as the second phase of mental hospital functions. For a long time institutions have stood for these two purposes: treatment and custodial care. Through the stimulus given more recently by Beers and his associates, we now generally accept a third opportunity or possible function in mental hygiene or preventive psychiatry, and now I would insist further that public state institutions have a definite responsibility in the field of teaching or education. The mental state hospitals and state schools for mental deficients constitute the proper and only laboratory for the proper study of psychiatry.

SUMMARY

(1) Discussion of problems of a state mental hospital involves consideration of its purposes and program.

(2) The fact that a state mental hospital touches and concerns a large percentage of the state's population, either directly or indirectly, is sufficient justification for it as a state agency.

(3) The highly specialized work of a mental hospital makes it important that its administration not be confused with other governmental functions and that it be clearly divorced from all political influence in order to pursue an even, uninterrupted, planned program.

(4) The successful administration and pursuit of an efficient, scientific program by a mental hospital depends in large measure upon selection and training of personnel. No other agency set up by government can so efficiently devise or operate a plan of selection of personnel or determine who shall serve as the hospital administration, itself more familiar than any other agency with the qualities and qualifications and requirements of this specialized service. This has no reference to the policy of government in resorting to civil service or any merit system in selecting general personnel of employees.

(5) Since the mental hospital problem of necessity stands to itself in contradistinction with other governmental functions, few people and few public officials have a sympathetic understanding of its problems except those either engaged in its service or immediately connected with treatment there. Therefore, a voluntary service and publicity agency in the form of public-spirited, well-known, prominent citizens has a great opportunity of rendering an invaluable service in keeping official and lay public advised and informed as to the program and needs of this type of public agency.

(6) Since psychology is physiology, and psychiatry is deficient or disturbed physiology, psychiatry becomes immediately a most important specialty in medicine. Failure to recognize this has at times allowed psychiatry to drift dangerously near the questionable cults outside or on the borderline of medicine. Psychiatry, therefore, must be promoted as a most important part of medical education in all reputable medical schools.

(7) Mental hospitals and institutions for mental deficients are the only laboratories for study and research in psychiatry. They should be teaching institutions not only for their own staff, but for schools of medicine and classes in sociology and abnormal psychology of higher institutions of learning.

(8) Therefore, I would lay out as a program for any well-administered and well-conducted

state mental hospital five definite functions to meet the public need of the day.

(1) Custodial care of chronic incurables.

(2) The proper hospitalization, study, diagnosis and treatment of all recent admissions.

(3) An extra-mural or field service, including a central clinic at the institution and branch clinics distributed through the state.

(4) A research activity devoted to study and investigation.

(5) A program of teaching, not only to include institution staffs, but students of medicine, classes in sociology, abnormal psychology, and so on.

DISCUSSION (*Abstract*)

Dr. Ralph M. Fellows, Osawatomie, Kan.—In this day and age, no attack upon any specific medical problem is thought to be well organized and complete unless it embodies three cardinal principles: prevention of the specific disease; intensive treatment of those sick with the specific disease; and follow-up care and study of those who have improved or who have recovered from the disease in question. It is true that certain types of mental disease are still thought by some to be incurable. Many other diseases, considered incurable a few years ago, have now been placed in the preventable or curable class. Typhoid fever, smallpox, pernicious anemia and diabetes are only a few of the specific diseases that a few years ago were thought to be fatal, but which have been conquered by the application of scientifically intelligent principles of prevention, intensive treatment, and follow-up care. It is not too much to believe that in the light of the present trend, as far as results in the treatment of mental diseases are concerned, that mental disease, too, may capitulate to some extent at least to methods of attack upon the disease that have given favorable results in other types of illness.

During the past three years, there has been a somewhat rapid development of new features and services at our own hospital. These developments embody the principles of prevention, intensive treatment, and follow-up care of patients. These new features and services direct the energies, advantages and abilities of the state hospital toward an increasing efficiency in prevention of and treatment of mental disease and delinquency.

In these three years there have been established and developed three separate outpatient facilities which operate one day each week for the staff of the hospital, cooperating with existing welfare and social agencies in the territory served by each of these three outpatient facilities. The arrangement in each case is fundamentally the same. The hospital furnishes at least one psychiatrist, a resident physician, a psychologist and a social service worker from the hospital. The county welfare boards and other existing social agencies which can be utilized furnish the services of a graduate nurse, secretarial help and physical facilities, consisting usually of reception room, consultation rooms, examination and treatment rooms. Case work in connection with these facilities is carried on by case workers on the regular staff of the welfare boards of the counties served by these clinics. To these outpatient facilities are referred patients who have improved sufficiently to leave the hospital on parole. Treatment necessary to continue their improvement in order that they may remain at home is carried out in this outpatient clinic each week. In addition to paroled patients, others in need of psychiatric help may be referred to this facility for psychiatric consultation. A great number of such referrals are children in need of child guidance. In this realm alone actual results, insofar as prevention of mental disease and delinquency are concerned, more than justify in dollars and cents the cost of operation, while the results obtained in preventing human heartache and misery and bringing about human happiness cannot be measured.

A great number of patients, adults especially, have never had to enter the hospital because of psychiatric care given at the outpatient facility. A large number of persons have visited these clinics to make inquiry concerning treatment for relatives or friends or to obtain advice about some aspect of mental disease or delinquency. A number of patients have actually been discharged from the hospital as restored through these clinics, because follow-up care and assistance in making social readjustment can be given through the combined efforts of the hospital staff and various county welfare boards, case workers, as well as other public agencies existing in the territory served by the hospital.

Patients with neurosyphilis are being seen much earlier than before, referred by case workers to these outpatient facilities, and they are consequently hospitalized (through voluntary commitment) with the improvement in results that ordinarily follows the application of early treatment in neurosyphilis. Paretics can be referred from the hospital to these facilities in some instances almost as soon as their fever therapy is finished for continuous treatment, which can be given weekly in the outpatient facility, thus providing the hospital additional empty beds once formerly occupied by paretics for occasionally as long as one or two years.

There is a distinct financial advantage accruing to the hospital from operation of these outpatient facilities. For example, in one instance twenty-nine patients were kept out of the hospital through one clinic for approximately ten and one-half months. At the regular per capita rate, it would have cost the State approximately $5,000 to have kept these twenty-nine patients in the hospital.

Precautions are arbitrarily set up through the limitation of intake and limitation of referring agencies in the facilities as well as facilities operated by the hospital by which we guarantee that no activity carried out by the hospital through these outpatient facilities can be interpreted as an infringement upon the private practice of neuropsychiatry.

During the time that these facilities have been in existence, the last one slightly over one year, 262 children and 148 adults, a total of 410 patients, have been cared for by them.

A considerable portion of this discussion, which, after all, is a discussion of state hospital problems, is concerned with activities in connection with child welfare. "The child of today is the inmate of tomorrow." It has been said that one child in every eighteen school

children in the United States will be an inmate of an institution, either correctional, penal or neuropsychiatric, if the present trend continues. Whatever steps can be taken toward preventing such conditions certainly are justifiable upon the part of any state hospital.

It is becoming more and more apparent to those concerned with the problems of human behavior, which problems certainly include mental illness and delinquency, that the foundation for a vast majority of cases of mental illness and delinquency is laid down in early childhood.

There are certain children whose illness or departure from normal behavior is such that they cannot be treated in an outpatient clinic while living at home. It does not follow that there is nothing to be done for them, but experience has demonstrated from time to time that if nothing is done for them they almost invariably become delinquent or mentally ill, eventually entering institutions.

One ever-prevalent reason for not doing more at a state hospital is "lack of funds." Here again, as in the three outpatient facilities, this service has been established without additional appropriation or without increase in the funds regularly appropriated for the operation of the hospital. A building on the grounds has been utilized; extra work by the staff has been contributed voluntarily without increased salaries; and in addition to this there have been volunteer workers, most of whom have academic degrees, who have spent many months working in this service for the invaluable training that such a unique situation furnished.

The A.M.A. continues to approve the hospital for resident training. Through these outpatient facilities in which children as well as adults are seen, and through the children's in patient service, resident physicians obtain a much more comprehensive training and experience in psychiatry than where the training is limited to a service with acute and chronic adults in the hospital alone.

The superintendent of the hospital occupies a modest position on the faculty of the University Medical School. This furnishes him the opportunity to give the medical student his introduction to psychiatry through a course in psychobiology in the second year. At present, third year medical students in groups of six spend at least two weeks in the hospital during the summer vacation as required work. With this introduction to psychiatry and with the demonstration that the principles of prevention, intensive treatment and social readjustment apply to psychiatry, as well as to other medical problems, the students are gradually becoming more interested in psychiatry, this interest being due in a great part to a changed attitude towards psychiatry.

It is thought that by adhering constantly to the principles of prevention, treatment and rehabilitation, the hospital has more nearly carried out its fundamental function, that of caring for people suffering from mental disease in the territory that this hospital covers. The staff, through its cooperative diligence, has brought about the rehabilitation of more sick people than ever before, actually increasing the turnover in the hospital 40 per cent. The staff has also contributed something to the existing knowledge concerning treatment of mental disease through research work. Outpatient facilities have been created which contribute something to the prevention and treatment of mental disease and delinquency.

The outpatient clinics have been in operation a comparatively short time, too short a time, actually, for the compilation of statistics on the results. However, the accumulation of statistics can only show the quantity of work done, cases seen, conferences held, intravenous injections given, spinal punctures made, psychometric examinations conducted, and so on. While this is important, it does not really reflect the actual accomplishments of these facilities. Of primary importance is the fact that a state hospital in a mid-Western state, through its cooperation with recently instigated social welfare agencies, has established facilities whereby the three cardinal principles of a scientific and intelligent attack on mental disease and delinquency can be carried out: prevention, intensive hospital treatment, and social readjustment.

The establishment of this activity alone is felt to be a distinct contribution to the medical and sociological culture of Kansas.

Dr. Lawrence Kolb, Washington, D. C.—Dr. Partlow is to be congratulated for bringing to our attention the undesirable hook-up that exists in so many jurisdictions between the mental hospitals and partisan politics and for suggesting the type of organization that would remedy this evil. So long as it exists we shall not be able to do away with many of the shortcomings of our public mental institutions. According to the Mental Hospital Survey Committee, partisan politics interferes with the personnel of mental institutions, either regularly or occasionally, in about twenty-two states. It is probably a tribute to our public men that interference is not more widespread, because in many states in which hospitals are fairly well administered from the public's standpoint the institutions are reasonably free from political interference. Dr. Partlow rightly places the creation of a non-political governing body for state hospitals as Problem No. 1. He also rightly places the selection of personnel as Problem No. 2, for without competent personnel responsible to a capable superintendent there can be no adequate treatment of patients, or even humane attention to their ordinary needs. Whether or not the employees are selected on a so-called civil service basis makes little difference, so long as they are selected in accordance with merit and have assurance of continuous employment during good behavior. It is of interest that only about ten states have civil service rules concerning employment of personnel and, of course, some states have no system at all beyond politics.

Large public organizations, such as the Veterans' Bureau, do not find it advantageous to train their nurses in institutions in which they serve; in fact, it has been found desirable to have a mobile nursing organization. Too much service in one place has a tendency to make some of us immune and impervious to new ideas, or at least indifferent to them. Nevertheless, in a small state organization it is doubtless necessary to employ nurses and attendants locally, rather than by transfer from other institutions.

Education of the public as to the needs, shortcomings and possibilities of our mental hospitals is a very important problem. Until this education is more widespread than at present we may expect these institutions to be neglected. It is unfortunate that in many places the mental hospital is something apart from general

social problems. Sending a patient to a mental hospital seems in the minds of a number of people the final solution. They then wash their hands of the matter, and never wonder whether these hospitals are what they should be and whether they are doing for the patients and for the general public what they might do. The interest of the public might be aroused if the hospitals engaged in extramural activities, using the hospitals as a center for mental hygiene activities for large areas, in this way making them useful as educational institutions as well as institutions engaged in preventive mental medicine. Until we improve the institutions and our technic for mental hygiene we cannot expect the public, or even the medical profession, to accept us as representatives of the most important specialty in medicine. In only fifteen states do hospitals have extramural activities. When a mental institution operates on a per capita cost of 32 cents a day it cannot do much more than house its patients, and if the public were properly informed no such disgraceful situation could long last anywhere. It is not possible with such funds to have a proper reception service, hydrotherapy, x-ray, or even decent clothing and food, and in poorly supported places it is no wonder that the superintendent is often more interested in raising hogs and potatoes than in the welfare and treatment of his patients.

I am glad that mention has been made of the desirability of research. It is a reflection on our intelligence that in this country we spend on public mental hospitals about $230,000,000 per year, and in those institutions do not spend $2,000,000 for research. This is a condition that should be remedied. There is doubtless in many places a nucleus for competent research organizations which, if properly supported, would eventually contribute much towards the discovery and remedial measures that would relieve suffering, as well as save expense in taking care of many mental patients.

Dr. Walter E. Vest, Huntington, West Va.—If a rank outsider to this Section may discuss Dr. Partlow's paper, I should like to say that he has not sufficiently emphasized two things. One is the lack of money. Dr. Kolb called your attention to the fact that you cannot run a jail on 32 cents a day. In West Virginia, the State allows 42 cents daily for feeding prisoners. I think my friends in the mental set-up in West Virginia house their patients for less than the amount allowed for food in the jails.

That is a disgraceful situation, and the key is not with the men who handle the institutions, but with the medical profession generally. Only the medical profession understands these things, and it is up to the medical profession to insist upon governments furnishing enough money to run these institutions properly. If the state medical associations would take this matter up, we could do much more than we do do. It seems to me that the problem in the management of state hospitals is primarily financial.

It is essential to have a merit system and to have tenure of office, but you have to have money enough to run the institutions before that can be done. The only segment of the population that can get these needs over to government and to the legislatures is the medical profession.

Dr. William Nelson, St. Louis, Mo.—It has been stated that the wealth of any community or the wealth of the world is dependent upon the brains or ingenuity of its citizens. I would have to subscribe pretty thoroughly to that concept, for I do not think it is so much the money we need as it is the intelligent spending of money. Just in the last two or three years a number of different localities in various states have appropriated large sums of money, running anywhere from two to twenty-five million dollars, for programs that include mental health problems, and so forth. It would seem we were getting somewhere from this immense amount of money that is expended if we consider the mere expenditure of money an indication of progress. As a matter of fact, I think the difficulty lies not so much in sources outside the men who are dealing with these institutions, but within the men themselves. That may seem somewhat critical to you. It may seem destructively so, but I do not mean it that way at all. Because we have an organization of men who are unacquainted with the character of mental illnesses, with the possibilities of treatment and so forth, I do not believe we can expect those bodies of men to go out and get a subscription of money for us in dealing with those patients without knowing something about what is done, and the medical profession generally is woefully ignorant of what the mental institution is and what is done in it. That is true today, as it was ten or fifteen years ago. So whatever improvement we get in a situation, we must think of it as being located primarily in the attitude of the people running these institutions, and the program of a broad public relationship in a community certainly is important.

So the whole thing comes back to our own door of enlightenment of the public in relationship to us through bringing forward a publicity program that will represent the institution as it really is.

Dr. Thomas H. Pargen, Jackson, La.—Some five years ago our hospital was in debt. A lot of the equipment was run down. At that time the medical service was separated from business management and a trained business manager installed. We know that forty or fifty years ago there was just "the doctor." He did everything. But with the more complicated problems coming, specialties have sprung up. We have surgeons, eye, ear, nose and throat men, gynecologists, and so forth, now. At that time, the mental hospitals were small. People lived simply, and one man could handle everything.

No man is capable of superintending the medical care of four thousand patients and tending to all the business angles of that institution at the same time. A trained business manager went in, the superintendent became the medical superintendent and supervised the medical care of these patients.

During the five-year period we have put in a forty thousand dollar hydrotherapy equipment, we have 400 more patients, we have built six more wards, the patients are well fed, well taken care of, better than before, and we have saved $270,000 on the same appropriation that we were getting five years ago.

Dr. Morris S. Wheeler, Rusk, Tex.—I think our problems may be considered in relation to our state government, the general public, and to our individual hospital administrations. Before the appropriations committee of our recent legislature, I was given eight

minutes for my personal appearance to explain the needs of my hospital for the next biennium, and that, of course, was not enough time. The solution to our problem seems to me to resolve into training and education, not only the training and education of our legislators, the men who run for office, but education of the public which expects us to give more and more service each year, and training and education within our own hospitals, with extramural activities, training of our nurses, employees, and our staffs.

HUMORAL ANTIBODY AND TISSUE TOLERANCE INDUCED IN POLLEN SENSITIVE INDIVIDUALS BY SPECIFIC THERAPY*

A PRELIMINARY REPORT

By MARY HEWITT LOVELESS, M.D.
New York, New York

HISTORICAL

Development of the Theory of Active Immunity in Allergy.—The clinical benefits which result from repeated administrations of the offending antigen to allergic subjects have been recognized for nearly three decades. The relative insusceptibility thus attained by the patient has been variously explained. Many allergists refer to their successfully treated patients as "desensitized," thus implying that hypersensitive man is analogous to the anaphylactic animal, and that the response to the antigen is curtailed in the treated patient because his antibodies are already more or less saturated with administered antigen. That such a mechanism might operate in allergic subjects was denied by Levine and Coca,[1] who found that the amount of unbound humoral reagin* was not reduced in patients during therapy, but might be definitely increased. Cooke, Barnard, Hebald and Stull,[2] and later Schmidt and Lippard,[3] using a quantitative Prausnitz-Kustner technic, likewise found that more antigen was often required to neutralize a patient's serum after treatment than had been required before therapy. Schmidt and Lippard believed this was due to an increase in humoral reagins during treatment. Cooke and his collaborators, on the other hand, postulated the development of a new immune body in the serum of treated patients to explain the altered behavior of post-treatment serum. Believing this induced factor to be an antibody which interfered with the antigen-reagin reaction in some manner other than through the binding of antigen by the antibody, they referred to it as an "inhibiting" agent. The theory of an active immunity, dependent upon the development of antibodies in allergic patients during therapy, gained momentum when Cooke, Loveless and Stull[4] succeeded in inducing a pollen antibody in nonsensitive subjects by means of injections of ragweed extract. A similar antibody was induced in sheep by Cohen and Nelson.[5] The induced antibody was distinguished from reagin by its incapacity to transfer sensitiveness to normal human skin. It resembled the hypothetical "inhibiting" antibody in its ability to interfere with the union between reagin and antigen. In studying the induced antibody further, the author[6] was able to show that, despite the belief of Cooke[2] and Harley[7] to the contrary, it bound its antigen in the manner characteristic of antibodies. Unlike reagin, it proved to be relatively thermostable. Believing that a similar antigen-binding, thermostable factor could be demonstrated in the serum of treated allergic patients if the reagin could only be eliminated in some way, the author experimented with the effect of heat upon serum until a temperature was found which would destroy all the skin-sensitizing capacity of a post-treatment serum without impairing its antigen-binding power. A water bath temperature of 56° C. maintained for from 2 to 5 hours, or of 60° C. maintained for one-half to 1 hour, fulfilled this requirement. By testing the passively sensitized cutaneous sites of normal subjects with antigen which had been mixed with heated serum, it was possible to show that treatment regularly induced an antigen-binding, thermostable antibody in human subjects regardless of whether they were naturally allergic to the antigen or were nonsensitive. In the light of this observation, the mechanism of the so-called inhibiting action of post-treatment serum could be interpreted as a simple antigen-antibody reaction, whereby antigen, which otherwise

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*Read in Section on Allergy, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

†From the New York Hospital and Department of Medicine, Cornell University Medical College, New York.

*The term *reagin* has been employed throughout this article to designate that immunologic factor (antibody?) which appears to develop spontaneously in many allergic patients following contact with the antigen and which is capable of sensitizing normal tissues passively to the homologous antigen. The term *antibody* has been reserved for that thermostable factor which (1) can be induced in nonsensitive or allergic subjects by means of parenterally administered antigen, (2) can bind the homologous antigen, but (3) is incapable of conferring sensitivity passively to normal human skin.

would have been free to combine with reagin, was bound and inactivated by the thermostable antibody. This finding strengthens the theory that induced antibody formation, rather than desensitization, is the typical response of allergic patients to parenteral administration of antigen, at any rate during the first year or two of therapy.

The Role of the Skin Test.—Although the value of cutaneous and of conjunctival testing with antigens is firmly established as an aid to diagnosis, the relationship between cutaneous and ophthalmic sensitivity on the one hand and the patient's clinical progress on the other is far from settled. It is interesting to note that early in the history of allergy, Noon[8] and his followers depended upon the diminishing susceptibility of their patients' conjunctivae to guide their therapy. Later Cooke,[9] Levine and Coca,[10] Rackemann[11] and Cooke and his collaborators[2] claimed that most successfully treated patients show no material reduction in cutaneous sensitivity. In contrast to this conclusion, Markin,[12] Grafton Tyler Brown,[13] Harley,[14 15] and Colmes and Rackemann[16] demonstrated with the scratch and puncture methods that distinct diminution and even loss of cutaneous response may occur during the patient's therapy; and Harley[7] confirmed this opinion using the intracutaneous method of testing in 1937. The conclusions of the above investigators would have been more convincing had successive tests been carried out with standardized antigenic solutions of uniform volume and had consideration been given to the influence of aging upon these solutions.* Neither cutaneous nor conjunctival reactions are being used commonly by American allergists as guides to the progress of patients under treatment.

PURPOSE

The aim of this presentation is to show that treatment of allergic patients with the offending antigen leads not only to clinical control of the disease, as is widely acknowledged, but also to the acquisition by the patient (1) of thermostable antibody in his serum and (2) of a diminished susceptibility of the tissues of the skin and eye to the antigen. In order to demonstrate and evaluate the tissue immunity, a special technic for quantitative testing at the threshold levels of sensitiveness of the skin and eye has been evolved.

METHODS

Preparation of Antigenic Solutions.—Ether-defatted pollen was extracted in alkaline saline solution and standardized upon the basis of the protein nitrogen content per ml. (10,000 P.N. units=0.10 mg. of phosphotungstic-acid precipitable nitrogen or, in the particular extract used, approximately 0.2 mg. of total nitrogen).

Collection and Titration of Serum.—Blood was taken from each of 23 Wassermann-negative, ragweed-sensitive patients previous to any test or therapy with pollen extract. After being separated from its cells by centrifugation, the serum was placed in rubber-capped vials, tested for sterility and then refrigerated until used. Specimens of serum were similarly prepared at intervals during and after the patient's subcutaneous therapy with ragweed extract. A portion of each specimen was subjected to a temperature of 60° C. in a waterbath for 30 to 60 minutes in order to inactivate completely its reagin without impairing its thermostable antibody. The antigen-binding capacity of each of these heated sera was then determined quantitatively by one of the two modifications of the Prausnitz-Kustner technic of passive sensitization which have been described in a previous article,[6] and which will be exemplified below.

Both methods are based upon the observation that when a mixture of reagin-bearing serum and of homologous antigen is introduced into normal skin, an erythema and wheal promptly result. If in some hours, after the "immediate" urticarial reaction has subsided, additional antigen is injected into the site, another urticarial response will be elicited providing the reagin was not completely neutralized by the antigen present in the initial mixture. By gradually increasing the antigen concentration in a series of such *in vitro* mixtures, it is possible to determine the smallest amount of antigen which suffices to neutralize the reagins present in the constant volume of serum. The skin-sensitizing potency can thus be expressed in terms of the antigen required to neutralize 1 ml. of serum.

As an example of this type of titration, readings are given below for an ante-treatment serum. R represents this reagin-bearing serum,

*Subsequent to the reading of this paper, the Cooke group[17] have reversed their stand regarding the effect of therapy upon the specific cutaneous response of pollen-sensitive subjects. Although errors due to variation in the method of standardization, age, and quantity of extract used for the cutaneous tests were not excluded, it was the conclusion of these authors that many of their cases of pollinosis showed a diminution of cutaneous response to the antigen following protracted treatment.

Ag the antigen in protein-nitrogen units per ml. of extract, NaCl physiological sodium chloride solution, and 0, +, ++, +++, ++++ the urticarial response elicited. One-tenth ml. of the following mixtures containing equal volumes of R, Ag and NaCl were introduced into normal skin:

	Immediate Reaction (Read in 15 min.)	Test with 0.02 ml. of 1000-Ag in 24 Hours
R+10 Ag+NaCl	+	+++
R+40 Ag+NaCl	+++	+
R+50 Ag+NaCl	++++	0

Thus between 40 and 50 units of antigen (ragweed pollen extract) were required to neutralize the skin-sensitizing reagins in each ml. of this serum, as indicated by the 24-hour test. At this point it might be stated that a large volume of this particular ante-treatment serum was on hand and it was therefore used as the source of reaginic serum for all titrations on the heated sera tested in this experiment, as follows.

When heated post-treatment serum containing thermostable antibody (represented by the symbol, T) was substituted for the physiological saline solution used in the above mixtures, both the immediate reactions and the 24-hour responses to additional antigen were affected, due to the antigen-binding capacity of the thermostable antibody. In other words, thermostable antibody to all appearances competes successfully against reagin for the common antigen. Before neutralization of the reagin in such mixtures can be initiated, antigen must be added in sufficient quantity to bind the thermostable antibody. Only excess antigen is available to the reagin. The extra amount of antigen required to effect neutralization of the skin-sensitizing power of such a reagin-antibody mixture, above that antigen required to neutralize the equivalent reagin alone, represents the quantity bound by thermostable antibody. Thus can the potency of thermostable antibody be titrated and expressed in terms of antigen.

The reactions produced in normal skin by mixtures of one heated post-treatment serum, antigen and the standard reaginic serum are indicated below:

	Immediate Reaction	24-Hour Test with .02 ml. of 1,000 Ag	
R+ 10 Ag+T	0 (Ag all bound by T)	++++	(Maximum Ag-R reaction. No R neutralized previously)
R+ 50 Ag+T	0 (Ag all bound by T)	++++	(Maximum Ag-R reaction. No R neutralized previously)
R+100 Ag+T	+ (Ag slightly in excess of T)	+++	(Large Ag-R reaction. Slight amount of R neutralized previously)
R+250 Ag+T	++ (Moderate Ag-R reaction)	++	(Moderate Ag-R reaction. Moderate amount R neutralized previously)
R+400 Ag+T	+++ (Large Ag-R reaction)	±	(Almost no R remaining unneutralized after "immediate" reaction)
R+500 Ag+T	++++ (Maximum Ag-R reaction)	0	(Ag of mixture in excess of T and R)

The immediate reactions may be used as an index to the presence of thermostable antibody, the heated serum listed above being capable of binding and completely inactivating approximately 50 units per c. c. of serum even in the presence of competitive reagin. In the present studies, however, the 24-hour end point (400 in the above titration) was employed in all instances. Although 40 units of this figure were actually attributable to the standard reaginic serum added to each mixture (*vide supra*), subtraction of this amount from the final readings was omitted inasmuch as it was constant in all experiments. In other words, the thermostable antibody content of the various post-treatment sera was judged by the total amount of antigen required to satisfy not only the heated serum under consideration, but also the constant volume of reaginic serum added.

Technic for Testing Skin and Conjunctiva.—In order to avoid the possible influence of a purely localized immunity dependent upon repeated inoculations into the same region, all therapeutic injections were given into the right arm, the left being reserved for intracutaneous tests. The strengths of extract selected for testing were such as to result in a series of responses varying from a definitely positive reaction down to a negative one. All tests were done in duplicate, one series being placed along the medial aspect of the flexor surface of the arm and the duplicate series being placed in a reverse order along the lateral border. The influence of location and of technical error was thus reduced. For most patients, extract strengths varying from 0.1 unit to 5 units per ml. of extract sufficed to reveal the threshold of cutaneous sensitivity when 0.062 ml. of each solution was intracutaneously introduced. It was feared, without subsequent justification, that confusing nonspecific reactions might be encountered because of the relatively large volume of extract arbitrarily used in the tests. A relatively large volume was selected in order to increase the accuracy of measurement, and any influence exerted upon the skin by the volume *per se* was

unimportant, inasmuch as it was constant in all experiments and since only relative change in the skin response of a specified patient was considered. Subsequent studies have revealed that 0.03 ml. of antigen, measured in an accurately calibrated 0.25 ml. syringe, is the most satisfactory testing dose for intracutaneous tests. Tracings were made at the height of the cutaneous reactions in all instances.

For testing the conjunctiva, one drop from a 26-gauge needle was the standard testing dose. The extract required to elicit slight erythema in the eye ranged from 10 to 10,000 units per ml. of extract. At intervals of 20 minutes, increasingly strong extract was instilled into the left conjunctival sac until the initial response was seen. The right eye served as a control.

An effort was made to perform all tests upon a given patient with extract of the same age in order to obviate the influence of aging which occurs in most antigenic solutions. When the extract available differed slightly in age from that employed in former tests, the age of the substituted extract was usually such as to discredit rather than fortify the conclusions of this investigation.

EXPERIMENTAL RESULTS

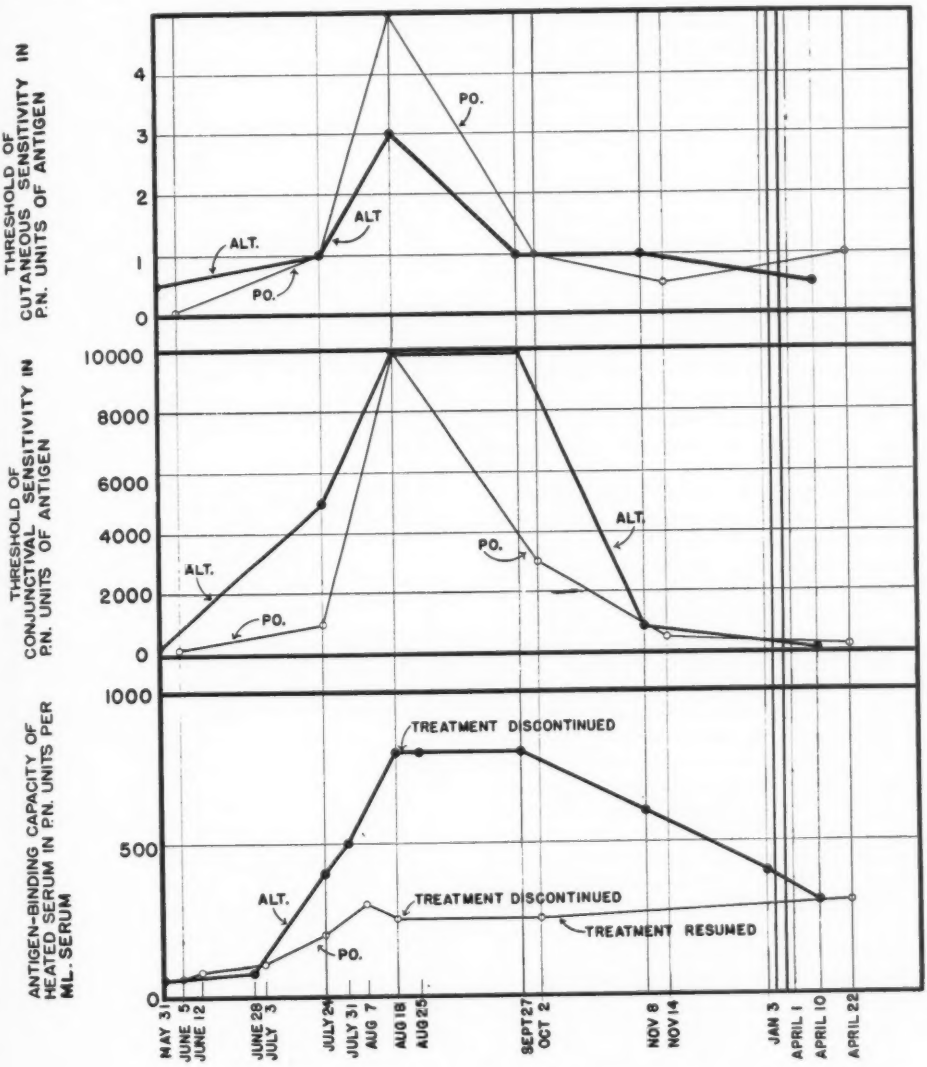
Detailed Description of Findings in Two Representative Patients.—The first patient, Alt, had no appreciable amount of thermostable antibody in her serum on May 31 before she had been tested and treated with ragweed extract. This is made clear by *Graph 1,* which shows that no extra antigen was required to desensitize the skin of a normal test subject when equal volumes of the stock reaginic serum, of heated Alt serum, and of 50 unit ragweed extract were introduced. In other words, Alt heated ante-treatment serum had no appreciable influence on the neutralization of reagin by antigen. (It will be recalled that the stock reaginic serum required nearly 50 units of antigen per ml. of serum to neutralize its skin-sensitizing reagins.) During a series of tests done upon this patient's eye, it was found that one drop of extract containing 250 units per ml. produced the first positive erythema. The threshold cutaneous response was elicited by 0.062 ml. of extract of 0.5 unit strength per ml. as indicated on the chart.

Shortly after these tests, therapy was begun, antigen being given twice weekly in increasing dosage. By the twenty-eighth day, a total of 1,300 units of ragweed extract had been given subcutaneously. When the patient's serum was heated and added to an equal volume of the stock sensitizing serum, in order to effect neutralization, antigen of 75 unit strength had to be added to the serum mixture, as tests in normal skin revealed. From this titration, it was concluded that thermostable antibody capable of binding 25 units of antigen per ml. of serum had developed in the patient's blood. On July 24, after an additional 26 days of therapy, the total dosage had risen to 10,000 units (equivalent to approximately 1 ml. of extract containing 0.2 milligrams of total nitrogen per ml.). In the presence of heated serum prepared at this time, 400 unit extract had to be added to the standard serum before neutralization was accomplished. Instead of 0.5 unit extract, as in the original test, 1 unit extract was now required to elicit the comparable response in the patient's skin and extract 20 times as strong as that originally sufficing was now found to produce the threshold response in the conjunctiva. Seven days later, on July 31, after a total dose of nearly 20,000 units, extract of 500 unit strength could be added to the mixture of heated serum and of the stock reagin-bearing serum before neutralization was effected. Another 2½ weeks of therapy brought the total dosage to 65,000 units and the top dose to 10,000 units. The neutralization requirement was now 800 units, or 16 times greater than originally found for the stock reagin-bearing serum. Even though the testing solution used for the tolerance tests at this time was younger than extract used in previous tests by 10 days, it was now necessary to use extract of between 1 and 5 units in strength (noted as 3 on the chart) in order to elicit the comparable threshold response in the patient's skin and 10,000 unit extract gave rise to the first reaction in her eye.

No further ragweed extract injections were given after these tests were done on August 18, near the onset of the ragweed pollinating season. A serum specimen obtained a week later showed no change in its thermostable antibody titer, but a second specimen prepared on September 27 after 33 additional days of exposure to atmospheric pollen likewise contained the same amount of antibody. At this time a slight increase in the susceptibility of the skin was perceptible, extract between 0.5 and 1 unit in strength eliciting the comparable threshold reaction. No change was noted in the threshold of sensitivity of the eye. After another six weeks without treatment, and a month after the ragweed pollinating season was over, this patient on November 8 manifested a 200 unit drop in the thermostable antibody in her serum, a cutaneous sensitivity not significantly changed from the previous test, and a decided loss in ophthalmic tolerance, 800 unit antigen now causing a visible conjunctival irritation. The patient reported a 75 per cent reduction in her usual hay fever symptoms during the 1939 season following her first course of injections. The patient has received no further pollen injections and study performed on January 3, 1940, showed a further drop in humoral antibody to 400. By April 10, 1940, the titer had fallen to 300, and the tolerance of the skin was ½ unit, whereas that of the eye was 250 unit extract.

A second patient, Po, responded to therapy with less striking serologic changes but with more marked tissue immunity than did Alt, as the graph shows. His ante-treatment serum similarly exerted no significant influence upon the neutralization requirement of the stock reaginic serum, as the chart will indicate. The threshold of susceptibility was located at 0.1 unit in his skin and at 200 units in his conjunctiva. After a week's treatment in which the patient received 175 units subcutaneously, approximately 75 units of extract were required to neutralize each ml. of the stock reaginic serum in the presence of an equal volume of the patient's heated serum. By July 3, a total dose of 1,000 units had been taken and 100 unit extract was now needed to complete the neutralization of the standard

reagin-bearing serum, thermostable antibody having been developed in the serum capable of binding about 50 units of antigen per ml. On July 24, after the total dosage had reached 5,000 units, the neutralization requirement had risen to 200 units and extract 5 to 10 times as strong as that originally sufficient was now needed to elicit a comparable threshold response in the patients' skin. A drop of 1,000-unit extract produced the same reaction in the eye as had been originally induced by 200-unit solution. Two weeks later, on August 7, after a total of 10,500 units had been administered, there was sufficient antibody in the patient's serum to raise the neutralization end point to 300 units. When another specimen was titrated 11 days later, on August 18, the neutralization end point was found at 250 units, following a total dosage of 16,500 units. By



RELATION BETWEEN TISSUE TOLERANCE AND CIRCULATING ANTIBODY

Graph 1

this time the cutaneous tolerance had risen to roughly 5 units and 10,000-unit solution was required to elicit the conjunctival response, despite the fact that the solutions used for testing were three weeks younger than those employed for the original tests previous to the patient's therapy.

The ragweed now being in pollination, no further treatments were given. After having gone through the pollinating season, the patient manifested no change in circulating antibody on October 2, the neutralization point remaining at 250. His cutaneous and ophthalmic susceptibilities had, however, increased (skin to 1 unit, eye to 3,000). Although a course of monthly injections was now instituted, the abrupt rise in immunity noted during the previous course of intensive treatment did not occur. The skin, a few weeks following the first monthly inoculation, gave the threshold response to ½-unit extract, the eye to 500-unit extract. Unfortunately, no serological study was carried out at this time (November 14). By April 22, 1940, the cutaneous reaction was obtained with 1-unit solution and the conjunctival reaction was positive to 200-unit extract. The serum required 300 units for its neutralization, indicating only a slight rise in titer as the result of the infrequent injections.

A more graphic conception of the cutaneous reactions of these two patients may be had by examining the tracings drawn during the successive tests, and reproduced in *Plates 1* and *2*. Above each set of tracings, the threshold of conjunctival sensitivity is indicated. Responses ranging from definitely positive to negative will be seen in most of the sets. The ideal way to compare successive tests with the first series of reactions shown by a given patient is to select the smallest reaction for which an approximate duplicate can be found in each of the succeeding groups. The strength of extract associated with this size of reaction may then be used as a basis for comparison. If the testing solutions are carefully graduated in strength, the reactions selected for comparison will lie close to the threshold of response in the skin. In Alt's tracings, for example, the 0.01 and the 0.1 unit reactions are not of a size found in tests subsequent to the first, but the 0.5 unit response seen in the initial experiment is suitable inasmuch as comparable reactions were elicited by 1 unit extract on July 24, by 1 and 5 unit extract on August 18, by 0.5 unit extract on September 27 after treatments had ceased, and again by 0.5 and 1 unit extracts on November 8. Similarly in Po's tests, the initial response to 0.1 unit extract was selected as the basis for comparison; 1 unit producing the comparable test on July 24, the 1 and 5 units test producing it on August 18 at

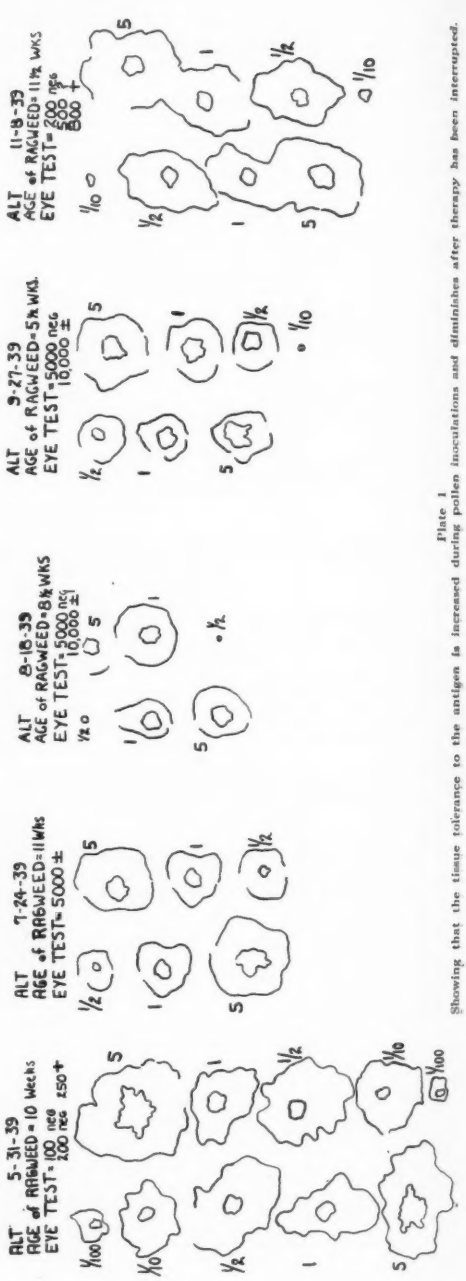


Plate 1

Showing that the tissue tolerance to the antigen is increased during pollen inoculations and diminishes after therapy has been interrupted.

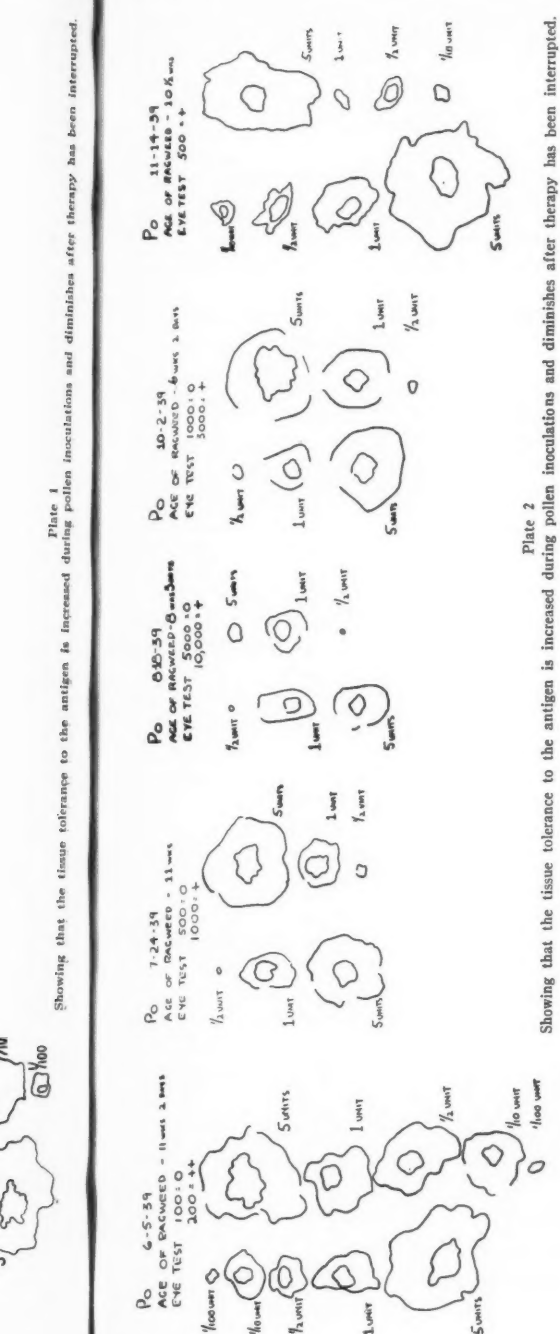


Plate 1

Showing that the tissue tolerance to the antigen is increased during pollen inoculations and diminishes after therapy has been interrupted.

Plate 2

Showing that the tissue tolerance to the antigen is increased during pollen inoculations and diminishes after therapy has been interrupted.

the end of the first course of treatment; the 1 unit test on October 2 and the 0.5 unit test approximating it on November 14. On April 22, 1940, 1-unit extract elicited the comparable reaction.

Because of the fact that numerous tests could be placed in the skin at one time whereas only one test at a time could be introduced into the eye, and also because the strength of extract required for the first conjunctival response was decidedly greater than that required for the skin, perhaps because of the wider area contacted by the small test dose, the fluctuations listed for the ophthalmic threshold of sensitivity in these two patients are seen to be much greater than those for the cutaneous threshold. Although the fluctuations noted in the ophthalmic threshold of sensitivity were larger than those of the skin, the general trend of reactivity in the eye follows that of the skin, and both follow fairly consistently the trend shown by the circulating thermostable antibody.

Summarized Report of Findings in 23 Ragweed-Sensitive Patients.—Studies similar to those described above for Alt and Po were done at intervals upon the sera and tissues of 23 pollen-sensitive subjects who received preseasonal therapy against ragweed pollen in 1939. However, only the results found at the beginning and at the end of treatment will be considered in this preliminary report. After 4 to 13 weeks of weekly or semiweekly inoculations, the 23 patients developed thermostable antibody capable of raising the neutralization requirement of the stock-sensitizing serum from its original neutralizing level to as high as 1,000 units of antigen per ml. of serum, as *Table 1* indicates. The threshold of response of the tissues to the antigen is seen to have been raised by treatment in most instances, some patients requiring, after therapy, the use of extract as much as 50 times stronger than that eliciting the threshold response previous to therapy. In order to complete the data, the top and total dosages administered each patient are listed, as is also the patient's estimate of his improvement during the 1939 pollinating season, comparison being made with previous years. Superficial analysis of the data given in *Table 1* shows that most of the patients developed circulating thermostable antibody, tissue immunity and lessened clinical susceptibility to the antigen as the result of their injections of ragweed extract. The figures in-

dicate that patients who developed definite circulating antibody, indicated by a titer of 150 or more in the table, acquired a heightened tissue tolerance to the antigen. It will be noted that the last three patients developed only a small amount of humoral antibody (enough thermostable antibody to neutralize 35 to 60 units of antigen per ml. of serum) and showed no change in their tissue susceptibility as the result of treatment. Although it is beyond the scope of this paper to investigate statistically the relation of humoral antibody to such factors as dosage and clinical improvement, it should be stated that the rate at which humoral antibody and tissue tolerance developed during treatment and diminished after cessation of therapy was subject to distinct individual variation. Likewise, the reported clinical improvement associated with a given dosage or with a given degree of tissue or humoral immunity varied from patient to patient.

Such observations do not necessarily condemn the theory that at least one mechanism of protection of allergic individuals against al-

Table 1

SHOWING THE RELATIONSHIP BETWEEN CIRCULATING ANTIBODY AND TISSUE TOLERANCE IN RAGWEED-TREATED HAY FEVER SUBJECTS

Patient		Titer* of Thermostable Antibody in Serum After Therapy	Increase in Tissue Tolerance** Resulting from Therapy		Therapeutic Dosage in P.N. Units		Clinical Improvement in Per Cent
			Skin	Conjunctiva	Maximum	Total	
1	Koc	1000	10-fold	10-fold	4,000	28,000	95
2	Bau	1000	2 "	10 "	4,000	24,500	25†
3	Alt	800	10 "	40 "	10,000	54,000	75
4	Bec	700	2 "	50 "	700	3,300	85
5	Gro	500	5-10 "	5 "	3,500	12,500	50‡
6	Kra	500	2 "	50 "	3,750	15,250	60
7	Dur	400	5-10 "	5 "	2,750	13,500	95
8	Kli	400	2 "	10 "	1,750	11,750	60
9	Haz	400	2 "	100 "	250	880	95
10	DeM	300	2 "	2 "	5,500	28,000	75
11	Po	250	30 "	50 "	2,500	16,750	90
12	Gros	250	5 "		3,500	12,500	85
13	Vog	200	2 "	5 "	4,000	11,250	80
14	Kut	200	5-10 "	12.5 "	500	2,690	75
15	Bel	200	10 "	2 "	3,300	13,000	60
16	Sie	200	50 "	30 "	1,100	2,780	90
17	Mal	200	2 "	6 "	5,250	10,000	85
18	Hen	175	5 "	20 "	2,250	5,750	
19	Lan	150	5 "	5 "	3,000	11,000	75
20	Mor	150	5-10 "	500 "	820	4,600	75
21	Ber	100	1 "	1 "	4,750	32,000	80
22	Car	100	1 "		1,500	5,200	0
23	Sbl	75	1 "	1 "	1,000	9,800	50

*Expressed in protein-nitrogen units of antigen. This figure includes not only the amount of antigen bound by 1 ml. of the heated post-treatment serum specified, but also the 40 units required to neutralize 1 ml. of the standard sensitizing serum involved in each of these titrations.

**Judged by the relative amount of antigen required for threshold reaction in the tissues (skin and conjunctiva) before and after the patient's first course of inoculations with ragweed extract.

†More sensitive by cutaneous test to iva axillaris than to ragweed pollen for which he was treated.

‡Patient was very pessimistic and before end of pollinating season was institutionalized for six months as a case of melancholia.

lergens may be the development of inactivating antibodies. It is obviously impossible for the patient or the physician to estimate accurately the influence not only of individual immunologic balance between reagin and inactivating antibodies, but of innumerable nonspecific and of undiagnosed specific factors upon clinical progress; since, also, other antibodies as yet unknown may be induced by so complex a foreign substance as pollen; and, finally, since little is known about the relationship of humoral to tissue immunity in these cases.

DISCUSSION

The data presented confirm the author's earlier contention that nonsensitizing thermostable antibody to pollen is induced in pollen-sensitive patients who receive adequate antigen parenterally. Immunologic studies of the serologic, cutaneous and conjunctival responses of 23 ragweed-sensitive subjects before and after therapy suggest that the acquired tolerance of the tissues is related to the titer of antibody induced in the blood stream through therapy. That the acquired immunity of the tissues is dependent upon the acquisition of thermostable antibody is strongly suggested by tests done in naturally sensitive skins.[6] By injecting such skin with heated post-treatment serum it was possible to abolish the cutaneous response of untreated patients to antigen. A definite but less striking diminution of the specific skin reactivity was noted in some untreated hay fever patients after they were transfused* with the blood of nonsensitive subjects who had received numerous pollen inoculations.

One may conservatively assert that three changes characteristically occur in pollen-sensitive patients during parenteral administration of pollen-antigen:

(1) thermostable antibody is induced in the serum;

(2) a relative immunity to the administered antigen is achieved as reflected by the conjunctiva and skin;

(3) clinical benefits result.

*To be published.

It seems logical to expect that the three might be referable to one mechanism, and that this mechanism may be dependent upon the binding of antigen by induced antibody. The exact relationship between acquired antibody and clinical protection will require further study for its establishment.

It has been amply shown that human and animal tissues are immediately irritated by the simultaneous presence of reagin and its homologous antigen. When antigen is bound by thermostable antibody, on the other hand, no detectable tissue irritation results. As a convenient working hypothesis, therefore, one may assume that hypersensitive patients develop allergic symptoms because of a reagin-antigen combination near their cells; that at least one means of attaining clinical tolerance may be the development of thermostable, and perhaps other as yet undescribed, antibodies which compete successfully against tissue reagins for the common antigen. If this theory is substantiated, we may have to replace the terms "desensitization" and "hyposensitization" with the word "immunization" when referring to the patients in at least the early stages of therapy.

The failure of the present studies to reveal a close correlation between the degree of humoral and tissue immunity on the one hand, and the acquired clinical insusceptibility of the patient on the other, may be attributable to the complex nature of the antigen and the probable multiplicity of resulting antibodies. It seems theoretically possible that a given patient might be clinically sensitive, for example, to one of the several antigens which must be present in ragweed pollen, and yet develop antibodies only to one or more of the remaining antigens. In this event, it would not be expected that the clinical results would be comparable to those obtained in a patient who developed antibodies to the antigenic components involved in his hypersensitivity.

It would seem that the use of the principle of quantitative testing in the region of the threshold of sensitivity of the skin and eye may eventually aid the allergist not only in the establishment of a diagnosis of sensitivity, but in the determination of immunity as well.

CONCLUSIONS

(1) A quantitative technic is described whereby the threshold of sensitivity to the antigen may be determined for the skin and conjunctiva of the allergic subject.

(2) While receiving pollen injections subcutaneously, pollen-sensitive patients gradually acquire (a) thermostable nonsensitizing antibody in the serum, which is capable of inactivating its antigen, (b) a relative insusceptibility of the skin and conjunctiva to the antigen, and (c) effective clinical immunity. Whether these represent related or merely parallel phenomena cannot as yet be finally stated, although the acquired immunity of the skin and conjunctiva is presumably due to the presence of thermostable antibodies in the tissues and the inactivation of antigen by these antibodies would be expected to play an important part in preventing allergic manifestations.

The author wishes to thank Dr. Horace S. Baldwin for his valuable advice and criticism, and Mrs. Margaret Schall, Miss Alice Stoll and Miss Ruth Ehrlich for their technical assistance.

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SYMPOSIUM ON MALARIA

REVIEW OF RECENT RESEARCH ON DRUG PROPHYLAXIS AND TREATMENT OF MALARIA*

A REPORT TO THE NATIONAL MALARIA COMMITTEE

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Panama, R. de P.

This is rendered as a member's annual report to the Chairman of the Subcommittee on Medical Research of the National Malaria Committee. The period covered is from September 1, 1938, to September 20, 1939, and the review includes only the literature received by our own local library and through correspondence as well as through contacts with local isthmian malariologists and scientific visitors passing through this region. Representative reports from various parts of the world have been used. Where the cost of the drug is not important and where mass treatment of the poor is not considered, "atabrin" seems to be the drug of choice. The consensus of opinion this year seems to indicate that some cases of malaria and malaria carriers cannot have their malarial infections "eradicated" by any form or length of treatment. Some of the newer forms of treatment will first be abstracted.

De Nunno[1] employed antimony tartrate, a 1 per cent solution in distilled water intravenously, on alternate days beginning with a dose of from 6 to 10 c. c. and increased by 2 c. c. to a maximum of 14 c. c. The total amount received by each patient was from 120 to 200 c. c. The number of patients in whose blood gametocytes developed were: 4 of the 6 untreated controls (66.6 per cent), 7 of the 12 treated with quinine (58.3 per cent), and 4 of the 40 treated with antimony tartrate (10 per cent). He concludes that after small doses of antimony tartrate the patient cannot infect mosquitoes.

Diaz de Leon[2] treated 15 cases of benign tertian malaria with sulfanilamide with completely satisfactory results. It was given in tablet form, except for a case that received one intramuscular injection. He considers sulfanilamide an effective specific drug for *vivax* infections.

Niven[3] treated 80 unselected cases of acute malaria in Kuala Lumpur with sulfanilamide (34 *falciparum*, 38 *vivax* and 8 *malariae* infections). As a control, 68 cases (30 *falciparum* and 38 *vivax*) were treated with quinine. Sulfanilamide, 3 grains a day, in two doses, for 7 days, was found to be less efficient than quinine. Five of the *falciparum* cases showed parasites at the end of the treatment, and 15 of *vivax* were still positive. Mosquitoes fed on four crescent carriers at the end of treatment were readily infected.

Read and Pino[4] believe that the sulfonamide preparations used in the treatment of tertian malaria have a poor specific antimalarial action because they have neither a sufficiently definite schizontocidal action nor a noteworthy gametocide action.

Farinaud[5] treated 322 school children that were malaria parasite carriers in Madagascar with "quinacrine" for five days followed by rhodoquine for 3 days. Some of the children received only one treatment, while others received a second course of treatment three months after the first. The blood was re-examined 15 days to a month after the completion of treatment. The percentage of children free of parasites after one course of treatment was 71 to 76 per cent and in those given two courses of treatment 94 to 96 per cent. A few children were refractory to treatment, but no gamete carriers were found following treatment. Dr. J. Lavergne, in discussing this report, stated that the synthetic drugs give better results than quinine.

Fastovskala and Chenderowitch[6] report on the use of two Soviet synthetic drugs and conclude that they are in every way as effective as quinine and can be recommended for mass treatment.

Tibourskaja[7] reports from Moscow the use of quinoline as a gametocide. In *vivax* infections 0.03 gram thrice daily eliminated subsequent infection of mosquitoes that were fed on the patient 24 hours after the last dose was given. In three *falciparum* cases daily doses of 0.09, 0.06 and 0.03 gram, respectively, produced a complete gamostatic effect. The duration of the gamostatic effect in *vivax* infections following 0.03 gram thrice daily was 5 days.

Dupoux, Marini and Barthas[8] carried out a mass prophylaxis in one of the most intensely malarious regions of Tunis. The experiment included 27,097 persons, of whom 10,021 were children from 0 to 12 years of age. The only drug used was "premaline" in tablet form. A tablet of this drug contains "quinacrine" 0.10 gram, rhodoquine 0.005 gram, and "praequine" 0.005 gram. The experiment started June 1, 1936, and the administration of the drug was continued till November 15, 1936. The tablets were given at intervals of ten days during the first month; thereafter twice a month. Adults were given three tablets and children proportionately smaller doses. Clinical relapses were very rare and even those who revealed some parasites were able to follow their daily occupations. Symptoms of intolerance were rare. The cost of the experiment worked out at 20 francs per head. This was only half the cost that daily quinine administration would have incurred. Twenty-one nurses administered the drug. The authors were enthusiastic about the results.

Ascoli's[9] method of treatment is well tabulated, on a series of nine reports, and those interested in further details regarding the treatment can secure references from the following table:

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*Read before the National Malaria Committee, meeting conjointly with the Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

†Director, Gorgas Memorial Laboratory.

Page	Author	Treated	Results and Remarks
35	Marciali, *et al.*	15	Splenomegaly in children. Satisfactory
565	Monaco, *et al.*	6	Very satisfactory in all
566	Acanfora	5	Chronic. Very satisfactory in all
568	Pizzillo	6	Acute, epinephrine with quinine. Very satisfactory in quinine-resistant infections
893	Milletari	70	Great value in splenomegaly and on patient's general condition
893	Mosna	9	Chronic splenomegaly. Good
893	Bell	6	Good results in all
895	Nucciotti	10	Primary attack treated with quinine, epinephrine. Several relapses
895	Nucciotti	6	Epinephrine, no effect on crescents

It would appear from this that the results of epinephrine treatment were usually good.

Field's[10] monograph contains an historical resume of cinchona and the progressive steps in the development of antimalarial drugs and offers the present resources for treating and preventing malaria by this means. The book is printed at Kuala Lumpur by the F. M. S. Government Press. The price is not mentioned.

Barbosa[11] records the results of treatment in 175 persons with primary infections and of 139 persons with reinfections of *P. vivax*. The treatment used comprised quinine alone, quinine and plasmochin, and "atabrin" and plasmochin. He concludes that treatment should not be prolonged more than seven or eight days. "Atabrin" associated with plasmochin is the choice in treatment to prevent relapse. He believes relapses of *falciparum* infections more frequent among children below 4 years of age than in later age groups.

Kalmus and Kostic[12] (Jugoslavia) report the action of plasmochin in reducing the number of relapses. See the following table:

Mode of Treatment	Quinine Sulphate	Quinine and Plasmochin Co.	Quino-plasmochin
Total cases	196	57	105
First relapse	51	4	7
Second relapse	8	0	1
Third relapse	4	0	0
Fourth relapse	0	0	0
Fifth relapse	1	0	0

Missiroli and Mosna[13] report on Schulemann's drug "cilional." It belongs to the plasmochin series of preparations and has the composition dialkylamino-alkylamino-oxy-quinoline. A dose of 2 centigrams a day for six days is a suitable therapeutic dose. Its action on the gametes of *P. falciparum* is quite as potent as that of plasmochin and in doses far less than any that produce toxic symptoms.

Overbeek and Gilbert[14] compare "atabrin" and quinine. Of 100 cases of benign tertian malaria, 53 were treated with "atabrin," 0.3 gram a day for five days, and 47 with quinine, 1.3 grams a day for seven days. There was no significant difference between the rates of action of the two drugs on the parasite, but three weeks after treatment 34 per cent of the quinine group harbored parasites as compared with 5.6 per cent of the "atabrin" group. One of the "atabrin" cases revealed an acute mental disorder which lasted fourteen days. A month later a second attack of malaria occurred: anxiety and mental confusion followed the use of 0.3 gram of "atabrin." The treatment was continued for three days, but fever and parasites persisted. The administration of 1 gram of quinine reduced the temperature to normal and the patient became more quiet.

Miyahara's[15] experience gained in Formosa by treating 30 cases of malaria with "atabrin," 0.3 gram a day for five days, led the author to consider "atabrin" no more effective than quinine in so far as the prevention of relapses is concerned. The parasite relapse rate was determined by the frequent examination of the blood, thick film method, during eight weeks following the end of treatment. The relapse rates follow: 62 per cent in the *vivax* cases, 12 per cent in the *falciparum* cases, and 7 per cent in the *malariae* cases.

Field, Niven and Guest[16] used "atabrin" musonate on a group of 284 patients (187 *falciparum*, 84 *vivax* and 13 *malariae*). This series was compared with a quinine group of 271 cases (184 *falciparum*, 77 *vivax* and 10 *malariae*). Each group was divided into two series so that intramuscular and oral methods could be observed. They concluded that as a *falciparum* gametocide "atabrin" musonate had no advantage over quinine. In spite of the efficacy of "atabrin" musonate in controlling attacks of malaria, the routine is not advised, since oral therapy is the method of choice in the majority of cases.

Rey[17] reports an experiment in an endemic area to sterilize carriers. The drug used was "atabrin" compositum in tablet form. Each tablet contains 0.1 gram "atabrin" and 0.005 gram plasmochin. It was administered on five consecutive days in one daily dose without regard to the time of day or interval from meals. The daily dosage was as follows:

Infants	½ tablet
1- 3 years	½ to 1 tablet
3- 5 years	1 to 1½ tablets
6-10 years	1½ to 2½ tablets
Over 10 years	3 tablets

Over a period of 8 months in 686 treated cases there was a relapse rate of 12 per cent in benign tertian malaria.

Sinton[18] describes some interesting changes that appeared to occur in gametocytes (crescents) during treatment with "atabrin" and suggests injury that might make them non-infective for the mosquito. Feeding experiments later showed that gametocytes even with little or no pigment in them could develop in the mosquito host.

Winchester[19] reports further experience in Georgia on the prophylactic use of "atabrin" and states that all of his cases showing parasites were of the *falciparum* species. Results were so encouraging as a control meas-

ure that he has decided to continue the method. No toxic symptoms caused by the use of the drug were encountered.

Bispham[20] states that if "atabrin" be used as prophylactic, soldiers can live and carry on their various activities in a highly infected area with a minimum of malarial infection and a maximum of effectiveness. Extremely few unpleasant reactions to "atabrin" occurred and these were of transient character.

Chopra and Basu,[21] in Calcutta, tested the effect of varying doses of antimalarial drugs on the infectivity of gametocyte carriers for mosquitoes. Laboratory bred *A. stephensi*, 4,665 in number, were used. Cinchona febrifuge, quinine sulphate, "malarcan," "tebetren," "atabrin," plasmochin and "gametochin" were the drugs tested. All failed, with the exception of plasmochin, to prevent the development of crescents in *A. stephensi*. Plasmochin in doses of 0.02 gram was effective in preventing this development.

Ciuca[22] and his staff report some malaria drug control experiments in both field and hospital practice. Four schizonticides were used (quinine, aristoquine, "atabrin" and "acriquine") and one gametocide (plasmochin). All three species of malaria parasites were represented among the cases treated. They report that the therapeutic efficacy of the drugs in the treatment of an attack were about equal, but that aristoquine was less effective than the others. They recommend, however, "atabrin" followed by plasmochin, each drug to have a five-day course. They think it unnecessary to administer daily doses of plasmochin in *falciparum* infections. A single dose of 0.02 gram, repeated every five days in the rare cases in which crescents persist, is sufficient to devitalize gametocytes. Children under 1 year of age do not tolerate "atabrin."

Gentzkow and Callender[23] believe that "atabrin" alone has failed to prevent relapses to a greater extent than any other of the treatments tried. Quinine, in large and long continued doses, was somewhat more effective in preventing relapse in *vivax* infections than is "atabrin" and markedly so in *falciparum* infections. Plasmochin given with or following "atabrin" has a pronounced effect upon the relapse rate in all types of malaria.

Chopra[24] treated four patients harboring *falciparum* gametocytes with "cilional." A total dose of 0.35 to 0.4 gram was administered in doses of 0 03 gram three times a day. This seemed to be sufficient to eradicate the gametocytes of *P. falciparum*. The opinion was offered, however, that plasmochin was preferable to "cilional." A smaller dose of the former is effective (0.02 gram daily for three days).

Sinton[25] tested the potentialities of "certuna" as a true causal prophylactic of *falciparum* malaria. Five patients were used in the experiment. The drug was well tolerated, but it failed in all five cases to prevent infection.

Muhlens[26] used "certuna" over a period of 2½ years in 113 cases of malaria. This drug is put up in tablets for oral administration. Chemically it is dialkylamino-oxy-quinolylaminobutane. When it was given in doses of 0.02 gram daily for 5 days he did not observe any toxic signs such as cyanosis or the formation of methemoglobin. He considers "certuna" superior to plasmochin as a gametocide in malignant tertian malaria.

Sioli[27] concludes from his use of "certuna" in inoculation malaria (benign tertian) that it is well tolerated and active, but that its activity differs from the action of quinine, plasmochin and "atabrin" in that a cure with "certuna," even in large doses, is not attained. It produces only a temporary suppression of the febrile attacks and parasites. He believes that the drug needs extensive trials in the field by tropical practitioners before its value can be determined.

Brachtel[28] reports some cases of malaria with remarkably long latent periods, with the object of drawing attention to the possibility of malaria in atypical febrile attacks. Latency period varied from 7 months to 1 year and in a single case 7 years.

Shute[29] discusses a series of non-immune persons who showed very long periods of latency and long-term relapse periods following treatment.

The summary of the experimental work of Ciuca and his co-workers[30] using "atabrin" follows:

(a) Of 4 subjects inoculated three times with sporozoites of *P. falciparum* (M. T. R. 78) and kept under the protection of a weekly dose of 0.30 gram of "atabrin" for 6 weeks, two showed clinical symptoms from 1 to 2 weeks after administration of the last dose of "atabrin." One showed a very mild frustrated infection. The remaining one did not show evidence of parasites in the blood during a 20-week period of observation. The control cases, inoculated once, showed clinical symptoms after a period of incubation lasting from 9 to 11 days.

(b) Of 6 subjects who were inoculated with sporozoites of *P. falciparum* (B. T. HOHR) and similarly treated, 3 showed clinical symptoms, but after varying intervals: the first one week after the last dose of "atabrin," two others after 6 weeks; the remaining three, a very mild frustrated infection during the period of administration itself. Of the three control cases inoculated with sporozoites once (and not given treatment), 2 showed clinical symptoms after a period of incubation lasting from 9 to 13 days; the third was immune and showed neither fever nor parasites.

In the circumstances governing our experiment, that is, repeated infections, the clinical protection afforded by "atabrin" was generally effective throughout the period of administration. The weekly "atabrin" method does not prevent infection by parasites.

The clinical symptoms began at varying intervals, starting from the first week after administration of the last dose of "atabrin."

The sporozoites of *P. falciparum* (M. T. R. 78) appear to be more sensitive to the action of "atabrin" than those of *P. vivax* (B. T. HOHR), and this confirmed findings reported previously (document C. H./Malaria/264).

If we compare the results obtained by the weekly method with those of the biweekly method (C. H./Malaria/265) the latter, which gives a total of 0.40 grain of "atabrin" instead of 0.30 grain, appears the better of the two. No prophylactic method applied to experimentally induced malaria succeeds in "eradicating" the infection.

As regards possible application in the field, both methods might achieve clinical protection

provided the number of reinfections did not exceed the range and relative efficacy of each.

Swellengrebel and de Buck,[31] after discussing malaria in the Netherlands and various methods of control, state that drugs have helped by eliminating the malaria patient as a source of anopheline infection, but there remain the healthy carriers against whom drugs are of no avail.

Clark and Komp's[32] ninth year's observations on malaria in Chagres River villages that are under drug control show much the same results as reported last year except for the last two months (July and August) of the year. The rainfall was extremely light this year and for a long time before the August survey all Madden Lake water was impounded and none escaped over the dam. The only river current by the villages was due to the discharge of water through the hydro-electric plant at the dam and the few small branches of the Chagres below the dam. This condition caused all floating vegetation to collect and remain in the river near the villages and anopheline breeding occurred on a scale that we have not seen since 1935, when a similar condition occurred at Madden Dam. Our malaria parasite rates in the river bank towns were five times as high as they have been for a very long period of time. Even though the drug has been in effect steadily, it did not prevent an epidemic. As soon as a normal river current is again established and floating vegetation is carried away, we believe that the anopheline density will subside to normal and that our village rates will also fall rapidly. Only one baby in 65 revealed a malarial infection during the year and this one was positive in its seventh and eighth months. The main increase in the parasite index during July and August was noted in the adults.

Treatment very often has to be placed in the hands of laymen and in these circumstances quinine is the safest and, for us, the cheapest drug for general use in rural regions and labor camps. Quinine is still our most important drug because of its clinical effectiveness and almost complete safety coupled with the years' widespread knowledge of its use and dosage. "Atabrin" is the drug of choice where expense need not be considered and where some form of supervision of treatment can be placed in effect.

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RECENT ADVANCES IN THE EPIDEMIOLOGY OF MALARIA*

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The Subcommittee on Epidemiology for 1939 has followed the practice adopted during the two previous years of briefly abstracting selected items of epidemiological interest in the world's publications (1938) on malaria. The titles covered totaled 335. This figure is doubtless incomplete, but comprehends the major output for the year. Of this number, about one-quarter (85) were predominantly epidemiological in content. These dealt mainly with the demographic and geographic conditions of malaria prevalence, parasite surveys in man and anophelines, the transmission significance of anopheline species and strains, the ovipositing and biting habits of anophelines, anopheline density, and with gametocyte production in man. It is hardly possible to compress into the limits of this report even the most salient facts recorded. Mention is made, therefore, only of contributions which seem to have general or unusual significance and application.

The most outstanding malaria publication of the year is undoubtedly "Malaria in the Netherlands," by N. H. Swellengrebel and A. de Buck,[1] of the Department of Medical Zoology, Institute of Tropical Hygiene, Royal Colonial Institute, Amsterdam. In this book the authors have presented the story of malaria transmission in Holland. They show that malaria was more prevalent and widespread in the Nineteenth Century than at present, and attribute the reduction to the extensive use of quinine. The present geographic distribution, annual and seasonal variations in malaria prevalence are noted, pointing out that malaria morbidity may not be a true gauge of malaria incidence. Large numbers of *A. maculipennis* were dissected; the results indicated that infected mosquitoes were found only in the fall months from September on, that sexual activity is suspended from early September to the following spring, but that biting continues until the beginning of November. It was then discovered that two genetically distinct biotypes of *A. maculipennis* exist in Holland. These are termed "short-wings" (*A. m. atroparvus*) and "long-wings" (*A. m. messeae*) by the authors. Both are infectible with Plasmodium, but while the long-wings hibernate commencing in September, the short-wings exhibit the behavior mentioned above and thus transmit malaria in the fall. The distribution of the short-wings is correlated with the presence of brackish water and corresponds with the present distribution of malaria in Holland. The habits of the two biotypes were carefully explored, especially as they related to malaria transmission. Both types evidently prefer lower animal blood and stables to human blood and houses. During the summer breeding season, sexual flights tend to prevent return to houses due to the strong attraction of the stables, but in the early fall while the long-wings hibernate, the short-wings discontinue long, sexual flights, and fly only for feeding purposes. This tends to keep them in houses, or stables as the case may be, and thus permits transmission during the fall months. The authors' experiments show that the autumnal infection of anophelines is responsible for the whole year's malaria, about one-third of which occurs during the autumn of the same year, the remaining two-thirds in the spring and summer of the following year. Their observations direct attention to malaria houses in which infected anopheline rest during the fall and from which they may escape in small numbers to neighboring houses. These clusters of houses containing infected mosquitoes are referred to as "foci of anopheline infection." The mosquitoes therein were shown to derive their infections more from healthy carriers than from those sick with malaria. Healthy carriers are more numerous among children than adults, thus houses with children in them are more liable to contain infected anophelines than those without. Various types of malaria control have been attempted. Drug control seems to have done as much as it can accomplish in Holland; its failure to eradicate malaria is due to the unrecognized parasite relapses of the healthy carrier. Antilarval measures (Paris green dusting and oiling) were partially effective, but too expensive. The reclamation of the salty areas by freshening would substitute harmless for harmful mosquito biotypes. This is mainly due to agri-

*Read before the National Malaria Committee, meeting conjointly with the Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

cultural and industrial rather than health pressure, but will be a very slow process owing to its magnitude and cost. Efforts at killing adult anophelines of all types wherever found did not produce any lasting decrease in the anopheline population, though the immediate results were good. Finally, species-sanitation in the control of adult anophelines was experimentally undertaken on the basis of the epidemiological information abstracted above. A solution of pyrethrum extract in kerosene was sprayed throughout the houses, mostly those with four or more children under 16, though houses with numerous anophelines were included irrespective of the age of the inhabitants. The houses were treated in late August, the middle of September, and the first week in October. The cost was approximately 15.5 cents per capita. Primary malaria incidence was reduced the following year to less than 10 per cent of its former level. In neighboring untreated villages, spontaneous reduction was not comparable. It is emphasized by the authors that this method, like drug control, does not destroy intrinsic malariousness of a region. Their ultimate hope for permanent malaria control consists in the freshening of the water in North Holland.

Home[2] gives an interesting account of malaria on shipboard. The vessel was in Dakar for nine days early in October. Mosquitoes were very abundant. From 5 to 32 days thereafter, 13 cases of malaria developed among the ship's company of 32; 2 cases were fatal. Meunier[3] writes of another epidemic on board a ship which left Ziguinchor with 17 officers and men. Twelve days later there were cases of fever on board. Four days thereafter she was forced to put into Algiers as 13 of the ship's company were down with fever. In 12 of the cases *P. falciparum* was found, in two of them associated with *P. malariae*.

B. Russell[4] studied malaria among the women and children of the Gold Coast. She advises that malaria is so prevalent among infants that she has adopted the practice of giving quinine to all children brought for treatment. The highest infection rate, 73 per cent, was in the three-to-six-months age group; in the less-than-three-months age group it was 36 per cent.

Mackay[5] shows that in Dar-es-Salaam, due to the complementary activities of two mosquito species, malaria is at a relatively uniform level throughout the year. Transmission is by *A. gambiae* during the rainy season and *A. funestus* in the dry season. Gametocyte carriers living near the edge of the town constitute a reservoir of infection for anophelines breeding near by.

Wilson[6] compares malariousness in a tribe living on the East African coast with that of another in central Tanganyika. The conditions of the first lead to hyperendemic prevalence with complete immunity as shown by reductions in spleen, parasite and morbidity rates in older children and adults. He estimates that each individual is likely to receive 12 infective bites per year. Anopheline control is economically infeasible. In the other tribe, immunity is incomplete, transmission occurring only 8 months out of the 12. The parasite rate is somewhat lower in adults than children, but the difference in spleen rates (87 per cent in children to 68 per cent in adults) is not marked. Adults suffer with malaria. The estimated number of infective bites per year is between 4 and 8. The author's conclusion is that in the first instance curative treatment should be avoided as far as possible, being resorted to mainly in the first two years of life only to save life without interfering with the acquisition of immunity. In the second case, he believes that drug or anopheline control is indicated by the circumstances. *P. falciparum* is the dominating species, immunity to which appears to be very temporary. The author describes certain morphological distinctions in *P. falciparum* in the blood of immunes (polymorphism) and non-immune (monomorphism).

Schwetz and Geronnez,[7] studying endemic malaria in several districts of the western Congo, find that in the areas of highest intensity (Mayumbe) infection appears within a few weeks of birth and within 6 months is virtually universal. The parasite index gradually declines after the fifth year. *P. falciparum* is the most prevalent species, *P. malariae* the second, and *P. vivax* least of all. They tend to drop out of the parasite picture in reverse order. *A. funestus* is the most prominent anopheline. In the lower Congo, the authors[8,9] found high incidence. *P. falciparum* was always much in evidence, though in some villages *P. malariae* was equally prevalent. *P. vivax* was variable in occurrence. *A. gambiae* was abundant in breeding places along the river. In Coquilhatville, which is also on the Congo, Schwetz and Baumann[10] found malaria to be feebly endemic. The parasite rate in children under 2 was low, higher in the 3-to-10-year-old group, after which it diminished until adult age, where it actually exceeded the infant parasite rate. *P. falciparum* pre-

dominated and *P. vivax* was absent. The common anopheline was *A. marshalli* var. *moucheti*. *A. gambiae* was not noted.

Afridi and Majid[11] have made a malaria survey of the Bahrein Islands (Persian Gulf), where the average annual rainfall is but 3.25 inches during 3 to 6 rainy days per year. Nevertheless, the climate is hot and humid. There are many warm, brackish springs. Malaria constituted about one-quarter of the cases treated in one of the large hospitals. The spleen rate of children varied from 13.1 to 38.9 in different towns, corresponding parasite indices amounting to 6.3 and 21.8. Five species of anophelines were found: *A. stephensi, A. fluviatilis, A. culicifacies, A. pulcherrimus,* and *A. sergenti*. Of these, *A. stephensi* was most prevalent and was the only species found infected. It is probably the only vector.

Russell, Menon and Ramachandra,[12] in reporting malaria conditions in the southern part of the Tanjore district of Madras Presidency, India, identified 12 species of *Anopheles: aconitus, annularis, barbirostris, culicifaces, hyrcanus* var. *nigerrimus, jamesi, pallidus, stephensi, subpictus, tessellatus, vagus* and *varuna,* of which *A. culicifaces* is the only effective carrier. Spleen, parasite, and gametocyte indices for the region as a whole were over 40, 30 and 13 per cent, respectively. Spleen and parasite indices were frequently greater for boys than for girls. About two-thirds of the infections were *P. falciparum* and somewhat less than a quarter were *P. vivax*.

Roy, Chandra and Siddons[13] note that while *A. stephensi* is abundant in Calcutta, it is not the dangerous malaria carrier there that it is in other Indian cities. They attribute this to the decided preference for bovine rather than human blood, as shown by a limited number of precipitin tests.

Ciuca, Ballif, Chelaresco and Lavrinenko[14] show that Roumanians are more susceptible to imported than to local strains of malaria.

Sarikjan[15] notes that in Central Russia infants and children suffer most from malaria. Most of the primary attacks in infants occur in the first half, particularly the second quarter of the year. This is probably due, according to the author, to the large number of prolonged incubation periods, but may be partly attributable to the biting of mosquitoes which have been hibernating.

Pinto[16] briefly reviews the spread of *A. gambiae* in Eastern Brazil. The species seems to be adaptable to water of many types and is still spreading. Sporozoite rates as high as 30 per cent have been found, accompanied by case-fatality ratios of from 6 to 15 per cent. The author believes it more likely that *A. gambiae* was transported across the Atlantic by boat from Dakar, West Africa, than by plane.

Rozeboom[17] records 17 anopheline species in Panama. Most of these are rare and have no malarial importance. It was found that *A. albitarsis* in Panama was not highly susceptible to *P. falciparum* infection, a fact which stands in marked contrast to the susceptibility of Brazilian strains of this mosquito to Brazilian *P. falciparum*. It was found that *A. albimanus* and *A. bachmanni* could be distinguished by differences in the frill of the mature eggs in the ovaries of the adult females. Over 80 per cent of 578 anophelines captured in houses were *A. albimanus*. On the other hand, over 90 per cent of 349 anophelines caught in small pig pens were *A. bachmanni*. The author comments that *A. albimanus* is still the most important vector in Panama.

Callender and Gentzkow[18] find the incidence of primary malaria to be three times as high in the United States Army in Panama as in employees of the Panama Canal. They believe this is due to the greater exposure and less immunity of the former group.

In Italian Somaliland, Cicchitto[19] found *P. falciparum* to be the most abundant parasite in hospitalized malaria patients. The percentage of parasite positives among those with splenomegaly was almost identical with the percentage of enlarged spleens among parasite positives. Splenomegaly was most frequent and intense in *P. vivax* infections.

Parrot and Catanei[20 21] studied the frequency of mixed malarial infections in an area in Algeria where for 17 months abnormal meteorological conditions prevented fresh infections. The blood of 1,878 persons was examined on 23 occasions. Of these persons, 311 were found positive at one time or another; 88 per cent of these had single infections. *P. falciparum* occurred in about 60 per cent, *P. vivax* in about 25 per cent and *P. malariae* in about 15 per cent. Thirty-seven persons had mixed infections with the following association of parasites: *P. falciparum* and *P. vivax* 25, or 68 per cent, *P. falciparum* and *P. malariae* 6, or 16 per cent, and *P. vivax* and *P. malariae* 5, or 13 per cent. All three species occurred in a single case. Malaria positives were twice as frequent below the age of 15 as above.

Premunition seemed to be developed at about the tenth year of age. Immunity to *P. falciparum* did not last as long as to *P. vivax* and *P. malariae*. Epidemics of estivo-autumnal malaria are, therefore, presumably due to the more ephemeral resistance to *P. falciparum*.

Martial,[22] studying malaria along the eastern frontier of Tonking and China, finds it most frequent in the vicinity of the limestone hills and most severe among the immigrant Annamite population. It is most prevalent in October and least so in March, temperature appearing to be responsible for the shift in intensity. When the temperature falls below 18° C., malaria incidence recedes; when it rises above 20° C., it increases. *P. falciparum* is responsible for 42 per cent of the cases, *P. malariae* for 33 per cent, and *P. vivax* for 25 per cent. Farinaud[23] states that malaria on the southern coast of Indo-China is not endemic. He finds that sudden increases in malaria morbidity have been accompanied by equally sudden increases in the number of such salt water anophelines as *A. sundiacus*, with *A. subpictus* and *A. sinensis* of secondary importance. Farinaud, Ramijean and Favot[24] have inquired into malarious conditions in Saigon and Cholon, the contiguous Chinese city. They found very low incidence. Spleen rates were all below 4 per cent, averaging 1.4. The parasite index averaged 2.9 per cent, varying up to 11.4 per cent. Six oriental species of Anopheles were found breeding in the outskirts of the city, *A. vagus* being the most numerous. In spite of the fact that this species is not a very effective vector, the authors feel that its large numbers may be responsible for the limited transmission.

Chedecal[25] found *A. vagus, A. hyrcanus sinensis, A. tesselatus,* and *A. aconitus* in horse stables in Hanoi. The first two species were most prevalent. Only 0.9 per cent of *A. h. sinensis* and 2.7 per cent of *A. vagus* contained human blood; nearly all the rest were precipitin-positive for horse blood. The attraction of horses for the local anophelines is believed to be of prophylactic value.

Lefebvre[26 27 28] gives malaria statistics for Laos, where malaria is hyperendemic except in the flood plains of the River Mekong. The mean parasite index of the country is about 43 per cent, the spleen index being 59 per cent. *P. falciparum* infections are the most frequent, with *P. vivax* coming next. In two northern provinces which border Burma, quartan malaria is more prevalent than tertian. Most of the population is infected early in life and because of repeated infections either succumbs to the disease or becomes immune to it. Clinical manifestations are relatively uncommon and not severe. Wherever *A. minimus* is abundant, malaria is frequent. In the high altitudes, *A. maculatus* may also be dangerous. *A. jeyporiensis* is of some importance in the northern part of the country and *A. leucosphyrus* is a lowland transmitter found mainly along the flood plains of the Mekong River. Malaria due to the last three species is characteristically seasonal in its occurrence, being correlated with the beginning of the rainy season, whereas malaria transmitted by *A. minimus* tends to be continuously hyperendemic.

Van Theil and Bevere[29] tested experimentally the preference of *A. maculipennis labranchiae* and *elutus* for human or pig blood. The procedure was to liberate mosquitoes in a large cage from which they could fly into but not back from smaller cages containing a man or a pig. In Holland, the local *A. atroparvus* preferred pig to man (12 to 1). In Italy, man was bitten by about twice as many *A. labranchiae* and *elutus* as the pig. Vargas,[30] working in highly malarious Temixco (Morelos, Mexico), found 67.6 per cent of 245 engorged *A. pseudopunctipennis* captured in houses to be positive for human blood. Of 420 females, given equal chances to feed on man or cow, 33 per cent fed on man; of 677 with man and horse equally available, 27 per cent selected man.

Huff[31] suggests that as all the biological participants in the malaria cycle are bisexual and are, therefore, subject to greater chance of variations than are unisexual organisms, it seems reasonable to assume that all three are undergoing a genetic change. He has already shown that susceptibility to certain avian plasmodia is an inherent genetic characteristic of mosquitoes which is inherited in a simple Mendelian fashion. If this could be demonstrated for anopheline mosquitoes it might be possible for the local anopheline species to change from a high to a low degree of susceptibility, or vice versa. In temperate zones where only a few individual mosquitoes survive the winter, this possibility might be especially important.

Russell[32] points out that where irrigation and malaria are associated it is faulty, improperly constructed and maintained irrigation that is responsible for the malaria hazard. Defects and faults are catalogued and the results of improper irrigation practice are shown.

Sinton and Shute[33] point out that the length of life of an adult Anopheles is of great importance in affecting its ability to transmit malaria. Previous information concerning longevity is reviewed and in addition their own observations are presented. This last consists of a number of experiments in which comparable groups of infectible mosquitoes are fed on malaria carriers and on clean individuals. No differences were observed in the mortality of the mosquitoes (*A. maculipennis atroparvus*) and the authors hold that death from plasmodial infection does not account for the failure of certain anopheline species to transmit malaria in nature.

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A REVIEW OF RECENT EXPERIMENTAL STUDIES IN MALARIA*

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In the following report an effort has been made to summarize briefly most of the work done in experimental malaria which was published in 1938 and some that has appeared in 1939. The fields of human,† simian‡ and avian§ malaria have been reviewed. Unfortunately space has not permitted more detailed consideration of many particularly interesting and significant contributions.

*Read before the National Malaria Committee, meeting conjointly with the Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*A report to the National Malaria Committee from the Sub-Committee on Medical Research.

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HUMAN MALARIA

In preparation of this section free use has been made of the *Tropical Diseases* Bulletin for references not accessible to the reviewer.

The results of two years' experience with malaria therapy in paresis were described by Bohls and Lawrence,[1] who used *P. vivax*. Of 68 patients treated, 7 died and improvement was noted in 76 per cent. In the ten years prior to the institution of malaria therapy, 90 per cent of the paretics had died, most of them within two years of admission to the hospital. Sioli, Kentenich and Boldt[2] also published a report describing their technic and results of malaria therapy.

Working with local and imported strains of *P. vivax*, Ciuca[3] and his colleagues found that persons inoculated exhibited greater susceptibility to imported than to local strains, but that infections with the latter offered some protection against the former. Maintenance of a local strain in a non-endemic country effected no change in the strain.

A rapid technic for the staining of thick blood films was devised by Simons.[4] Matumoto and Hirasiki[5] described a method of staining large numbers of slides.

The relationship of parasite density to clinical activity in primary vivax attacks has been studied by Boyd.[6] He noted that clinical activity due to *P. vivax* may be initiated by densities of 10 per c.mm. or less. Excluding a few days after the onset, the duration of clinical activity does not exceed the period in which the density remained at 100 or more c.mm. Attacks following trophozoite inoculation terminated with higher parasite counts than did those induced by sporozoites. Rarely were counts of 500 or less noted at the conclusion of an attack. Sivalingam[7] also studied parasite densities in primary and "subsequent" attacks of vivax malaria. He observed higher counts in the primary attacks and their association with higher temperature elevations. This relationship was not noted in the secondary attacks. He concluded, surprisingly, that about 900 parasites per c.mm. were necessary to produce fever in primary attacks and about 500 in subsequent attacks.

Mayne and Young[8] observed what they interpreted to be an antagonism between *P. vivax* and *P. malariae* in patients inoculated with both species. Parasites of one species usually dominated the picture at a given time.

Additional papers on Henry's reaction have been published. Trenz[9] described a modified technic. Chorine,[10] in a fine description of Henry's reaction, states that it is not due to the presence of antibodies in the serum; that the intensity of the reaction may vary from day to day in the same serum kept on ice; that it occurs only in distilled water or hypotonic solutions; melanin serves only as an indicator; the chief role is played by euglobulins; malarial euglobulins have no special affinity for melanin; the melanin reaction is abolished by a temperature of 55° C. for 30 minutes; the reaction becomes positive 3 to 5 days after infection of malarial blood for therapeutic purposes and is of value clinically. Sicault and Messerlin[11] described a new technic for a graduated melanoflocculation test.

That "atabrin" may produce morphological changes in falciparum gametocytes has been demonstrated by Sinton.[12] Such altered gametocytes apparently were still capable of infecting mosquitoes though they produced atypical ookinetes and oocysts. The chief effect of the drug was to cause a diminution, or loss, of pigment. Sinton and Shute[13] found that infection of *A. maculipennis* with *P. vivax* appeared not to shorten the insect's life under favorable conditions, but may do so under unfavorable conditions. Inability of some species to transmit the infection is thus not due to death as a result of the infection.

Boyd and Kitchen[14] found that when exflagellation of vivax microgametocytes is demonstrable, a significantly higher proportion of lots of mosquitoes applied show infection rate in excess of 75 p. c. than when it was not noted. Similarly with falciparum a greater proportion of lots showed 65 p. c. or higher infection rates when exflagellation was observed. Both exflagellation and higher infection rates in mosquitoes were more commonly noted in the spring and autumn quarters. These authors[15] have also observed delayed clinical activity due to *P. vivax* in three patients who had originally been inoculated by both *P. vivax* and *P. falciparum* and whose primary attacks were characteristic of *P. falciparum*. The secondary attacks occurred in the winter or spring months 235, 236 and 282 days, respectively, after the onset of the primary attacks. In another study[16] the effect on the course of vivax and falciparum infections of quinine administered on a single day only was investigated. It was found that a single dose of 20 grains had little effect on falciparum infections, but that single doses of 11 or more grains usually suppressed vivax paroxysms for varying periods, particularly if the attack had already proceeded for 8 or more days. The same authors[17] were able to demonstrate vivax sporozoites in Giemsa-stained sections of tissue removed from the site of inoculation by infected mosquitoes in one of three cases, but such excisions did not prevent the development of malarial infections. In one of four other biopsies, in which regional lymph nodes draining the area of inoculation were removed and sectioned, characteristic sporozoites were again demonstrated. These workers[18] noted an apparently authentic instance of a 304-day incubation period in a patient inoculated therapeutically with *P. vivax*. During this period he had been on a screened ward and there had been no autochthonous malaria in the institution for two months prior to the onset of this attack. When the blood was inoculated into another patient, recovered from an infection with the same strain as was used for the inoculation of the first patient, a complete homology was indicated. Studying the clinical reaction of the first and last of many series of three patients, each of the three being inoculated with identical vivax-infected mosquitoes (excepting for intervening deaths of some), differences were noted.[19] Patients last inoculated in the series tended to have longer incubation periods and shorter attacks. When many mosquitoes were used, these differences were eliminated. The duration of the clinical attack following application of a moderate number of infected mosquitoes tended to vary inversely with the duration of the incubation period.

Boyd and his associates have also made the following contributions: they[20] have shown that the simultaneous inoculation of equal quantities of trophozoites of two strains of P. *vivax* and resulting infections provide a subsequent deficient immunity to either strain; determined[21] that during the incubation period, at the time of the acute primary attack, or shortly after recovery

from the primary attack, an absence of cross immunity between *P. vivax* and *P. falciparum* infections exists; found[22] that by daily subinoculation of 10 c. c. quantities of blood from a mosquito-inoculated patient to other patients parasites may be demonstrated in the blood of the donor at least three days before they are detected in the thick smears, using both a Mexican and Florida strain of *P. falciparum,* it was noted[23] that *A. quadrimaculatus* originating and reared in Florida were much better vectors of both strains than were *A. pseudopunctipennis* of Mexican origin; homologous immunity to *P. vivax*[24] was demonstrated to obtain 7 years after the original attack without intervening re-inforcement. It was greater in degree when re-inforced at the end of 4 years.

Azzi and Del Frade[25] examined the sera of twenty children with malaria and with no evidence of syphilis, using the Meinicke and Kahn tests. Fifteen children had falciparum and five, vivax infections. They concluded that malaria may give positive reactions during an attack of fever. Kitchen, Webb and Kupper[26] made a detailed study of the Wassermann and Kahn reactions before, during and following 25 naturally induced malarial infections in nonsyphilitic persons. Positive reactions developed in each instance. In one instance a positive reaction and a considerably increased cell count was noted in the cerebrospinal fluid. The first positive reactions were observed both before and after the period of clinical activity in a few instances, but in 68 per cent of the attacks they occurred during the first two weeks of the febrile stage. The relative number of positive reactions was greater in vivax than falciparum infections, among females than among males and up to 35 years than over that age.

Following a clinical investigation of vivax malaria, Lotze[27] made a number of observations. There is no salt retention; quantities of vitamin C, greater than normal, are utilized by the patient; serum albumin is increased and serum globulin decreased; Wassermann and flocculation tests were positive; the blood picture resembled that of pernicious anemia with a hypochromic index. He discussed vitamin C therapy in malaria.

Hegner[28] found that vivax merozoites had a special affinity for reticulocytes, but that falciparum and malariae parasites invaded older cells. Malignancy of falciparum is partly due to this characteristic and partly to its multiplication rate, while the slower rate of multiplication of *P. malariae* renders it less virulent. He believes that the large size of the vivax-infected erythrocyte is not due to an increase in size, but rather to the invasion of reticulocytes which are larger. Kitchen[29] found the percentage of reticulocytes infected much greater than that of mature red blood cells throughout the course of two vivax infections. Multiple infections were more numerous in reticulocytes. In about three-quarters of observations actual numbers of infected reticulocytes were greater. The author found that Wright's stain could be satisfactorily substituted for brilliant cresyl blue in staining reticulocytes. Hingst[30] believed that proportions of reticulocytes and mature cells infected with *P. vivax* as determined from peripheral blood smears does not give true values of actual conditions, since most of sporulation occurs in the internal organs. He also considers multiple infection to be rare except with certain strains of *P. vivax* and that it is there due to amitotic division of parasites. Kitchen[31] observed that in three falciparum cases, infected mature erythrocytes were always found and always exceeded numerically the infected reticulocytes which were noted in 70 per cent of observations. The two types of host cell alternated irregularly, however, in exhibiting the higher rate of infection. *P. malariae* was always found in both greater relative and absolute numbers in mature erythrocytes. Vyronis[32] likewise found that *P. vivax* showed a predilection for reticulocytes and attributed it to the stickiness of the immature forms.

SIMIAN MALARIA

Studies on the skins of normal and immune spider and *Cebus* monkeys with *P. brasilianum* infections (as well as similar studies on canaries) led Taliaferro and Bloom[33] to conclude that any antibodies which might have been present were in too low concentrations in the skin of immune animals to accelerate the macrophagic response to injections of malarial blood. Studying extra-abdominal spleen in monkeys having infections with *P. cynomolgi* and *P. knowlesi,* Afridi[34] found changes in spleen size during the infections similar to those earlier found by Coggeshall.[35] Maximum splenomegaly occurred 1-4 days after the crisis in *cynomolgi* infections. In *knowlesi* infections splenic enlargement was more rapid early in the disease and less marked at the time of the crisis. Irregularities in segmentation were evident during crisis.

Specific agglutinins were found by Eaton[36] in the sera of monkeys infected with *P. knowlesi* between the fifteenth and forty-fifth days after onset of the infections. These antibodies increased in titer as the infection subsided, and persisted for 1 year or longer in monkeys having chronic infections. They were effective only against mature parasites. Coggeshall and Kumm[37] superinfected monkeys carrying chronic *P. knowlesi* infections and studied the corresponding changes in protective antibodies of these animals as compared with monkeys with chronic infections which were not superinfected. The former group received at approximately 7-day intervals 7 injections containing from 5 to 7 billion parasites. The protection tests were done by inoculating from 1 to 1.5 millions of parasites, followed by daily injections of pooled immune serum. The protective value of the serum of the superinfected group of monkeys was much higher than that of the group of unaltered chronic infections. When 9 further superinfections were made the protective antibodies disappeared, but in 8 out of 10 of these monkeys the protective antibodies reappeared following a month's rest and then a single superinfection. The decrease in protective antibodies following too intense superinfections, they believe, may possibly be due to the exhaustion of the specific antibodies by the tremendous quantity of parasites. Coggeshall and Eaton[38] infected monkeys with less than 10 parasites of *P. knowlesi* inoculated intraperitoneally. There was an inverse relationship between number of parasites in the inoculum and length of incubation period, but once established, the severity of infection was independent of the size of the inoculum. A direct correlation existed between the size of the inoculum and the amount of immune serum necessary to prevent death of the monkey. Infection was prevented when the inoculum was small and the amount of protective serum was large.

Complement-fixation has been demonstrated in rhesus monkeys infected with *Plasmodium knowlesi* by Coggeshall and Eaton.[39] Antigens were prepared either from

spleens of monkeys with heavy infections or from blood containing large numbers of parasites; the latter produced the best antigens. The complement-fixing antibodies appeared early in the acute infections, then decreased in amount, and persisted through the chronic infection. During the chronic infection the titers fell before and rose following the parasitic relapses. Wide variation existed among individual monkeys in antibody response. Some produced antibodies of very low titer, while in others the titer was as high as 1:64. While there was an apparent positive correlation between the titer of complement-fixing antibodies and the degree of protection afforded by the serum, there were cases in which the former was low and the latter high and vice versa. Eaton[40] has demonstrated a soluble material antigen in the serum of monkeys infected with *P. knowlesi.* The antigen was labile to acids and alkalies, was not destroyed at 56° C. and was precipitated by ammonium sulfate. During the acute infection the amount of antigen was related to the parasite count. Specific complement-fixing antibodies resulted from injection of the antigen into normal monkeys. These antibodies would react with antigens extracted from parasitized cells, as well as with the antigens occurring in the serum as a result of the infection. The antigen was incapable of evoking an immunity to infection.

Monkeys which had been cured of their *knowlesi* infections retained sufficient immunity to prevent death following reinoculation as late as 3 months after the cure (Coggeshall[41]). The same persistence of immunity against *P. knowlesi* was found in human patients. (Ciuca, Badenski, Jonescu, Tiriteneau;[42] Milam and Coggeshall.[43]) On the other hand, Shortt, Pandit, Menon and Swaminath[44] found that monkeys cured of their infections of *P. cynomolgi* and *P. knowlesi* lost their immunity to reinfection by homologous strains of parasites.

Taking advantage of the high susceptibility of rhesus monkeys for *P. knowlesi,* Milam and Coggeshall[43] studied the duration of these infections in human patients by repeated inoculations of patient's blood into monkeys. In 30 white patients the parasites were seen in the blood smears as early as the third and as late as the eighteenth day after inoculation. The blood was non-infectious for monkeys as early as the eighteenth and as late as the one hundred and thirty-first day following inoculation. Negroes were less susceptible, their blood being non-infectious for monkeys as early as the twenty-eighth day and remaining infectious only as late as the thirty-sixth day. Of particular interest is a white patient who was shown to have a latent infection 114 days after his blood had ceased to be positive by thin and thick smears. Success in obtaining a good test antigen for complement-fixation in simian infections of *P. knowlesi* also made possible the study of complement-fixation in human patients infected not only with this parasite, but with *P. vivax* and *P. falciparum* (Eaton and Coggeshall[45]). In making their tests on the sera of patients, many of whom were paretic, it was necessary to eliminate any non-specific reactions introduced by the syphilitic infections, as well as the effect of hetero-agglutinins for normal monkey cells in certain human serums which might fix complement. With one exception the malarial antigens were no more reactive with Wassermann-positive than with Wassermann-negative sera. With an antigen prepared from dried parasitized red cells by extraction with saline, freezing and thawing, they were able to demonstrate strong complement-fixations with the sera of patients infected with *P. vivax* and *P. falciparum,* as well as with *P. knowlesi.* Hence the complement-fixing antibodies in malaria are group-specific rather than species-specific, differing in this respect from the protective and agglutinative antibodies. Milam and Kusch[46] have studied 35 paretics infected with *P. knowlesi.* All 29 of the white patients were susceptible, but there was practically no infection in 6 negroes. Following an incubation period of 4 to 6 days, a quotidian fever appeared and lasted for about 10 days. There usually was spontaneous recovery. In three patients with no previous malarial history relapses occurred on the twenty-third, thirty-third and forty-third days after inoculation. In four cases of relapse, inoculation tests into monkeys were not followed by infection, indicating that the relapses were probably due to latent infections of *P. vivax.* The authors believe that *P. knowlesi* should not be considered harmless to man, since in three cases there were sudden increases in parasite numbers sufficient to be dangerous. The infection is effectively cured by quinine. The infections produced improvement in the paretic condition of 48 per cent of the cases.

Coggeshall[41 47] found sulfanilamide to be effective prophylactically and therapeutically against *P. knowlesi* infections in rhesus monkeys, while sulfanilyl sulfanilate had no prophylactic action and slight therapeutic action. The former was toxic for the parasites *in vitro,* but the latter had no observable effect. Doses as large as 3 c. c. were necessary to check chronic infections, a result which was also found by Das Gupta and Chopra.[48] Soluseptasine has also proven to be effective against *P. knowlesi* infections in monkeys, doses of 2 c. c. (5 per cent aq. sol.) being sufficient to bring about rapid disappearance of the infection (Chopra and Das Gupta[49]). Singh and Singh[50] treated 8 rhesus monkeys with 2-sulphanilyl-aminopyridine. Given in massive doses (total of 9 grams) the blood was freed from parasites on the fifth day. The drug was effective in decreasing the number of parasites in the blood and in removing the infection entirely, as shown by inability to provoke relapse in the treated animals or to infect normal animals with their blood. No toxic symptoms were observed. Chopra and Das Gupta[51] were able to bring about the same result with 5 daily intramuscular injections of an oily suspension containing 0.15 grains of this same drug. Christophers and Fulton[52] found that while 1:11 normal undecane diamidine had curative action on *P. knowlesi* infections in monkeys, the drug was toxic and the effect uncertain.

The parasite, *P. knowlesi,* has proven to be especially suitable to physiologic studies, particularly to studies upon the respiratory metabolism. The oxygen uptake by the parasite was found to continue practically undiminished for some time in the absence of added glucose. There was indication of reduction of oxyhemoglobin by the parasites. Oxygen was consumed with an approximately equal output of carbon dioxide, non-protein nitrogen was increased, but there was no observed increase of ammonia (Christophers and Fulton[53]). Certain antimalarial drugs caused an inhibition of the oxygen uptake by the parasites, which was capable of being expressed as a coefficient of inhibition. There was a suggestion of parallelism between therapeutic effect of the agent and the inhibitory effect upon oxygen uptake (Fulton and Christophers[54]).

Mosna[55] tried out the African monkeys, *Papio cyno-*

cephalus, Cercopithecus, griseo viridis and *C. cephus,* as possible hosts of *Plasmodium knowlesi.* While all were susceptible to infection and while *C. griseo viridis* seems to be a better reservoir than rhesus monkeys, he concludes that none of the species tested could replace rhesus monkeys for laboratory work. Rodhain and Muylle[56] inoculated human patients with the blood of chimpanzees infected, respectively, with parasites resembling *P. vivax, P. falciparum* and a mixture of these two. The fact that the patients failed to contract infections adds to the previous evidence that the parasites of the chimpanzee are distinct from those of man.

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James,[57] Manwell,[58] Kikuth,[59] and Rodhain[60] have further identified and attempted to clarify the nature of the so-called exo-erythrocytic forms occurring in *Plasmodium gallinaceum, P. circumflexum, P. cathemerium* and *P. relictum.* These forms are generally considered as being non-pigmented and to be present both in leukocytes and in fixed reticulo-endothelial cells, passing through a definite cycle of schizogony. Strains are obtained from birds infected with sporozoites and may then be passed on by blood inoculation. Kikuth[61] found the organs of a bird that had been inoculated with sporozoites infective within 24 hours of the original sporozoite inoculation. This, he thinks, indicates the presence of non-pigmeated forms in the internal organs, and he considers them transition forms of sporozoites. Corradetti,[62] however, does not think exo-erythrocytic forms are developed directly from sporozoites, since they also occur in birds inoculated with infected blood. He compares the parallel behavior in the schizogonic cycle of these forms in reticulo-endothelial cells with that of regular pigmented parasites in red blood cells.[63] Manwell finds no essential difference between parasite forms found in erythrocytes and those found elsewhere. Hegner and Wolfson[64] [65] have found parasites in cathemerium infections which resemble toxoplasma. More work can be expected on determination of the exact nature of exo-erythrocytic forms.

Hegner and Eskridge[66] protected birds by passive immunity, injecting prepared "immune" serum from birds suffering from active and sub-patent infections of *P. cathemerium.* However, protection was manifest by modifying symptoms and pathology rather than lessening the invasive power of the parasites. Redmond[67] concluded that cross immune relationships in strains of *P. cathemerium* and *P. relictum* varied according to the degree of virulence of each strain, the most virulent producing the most effective cross immunity. Manwell[68] tested for cross immunity with a number of species and surmised that morphological similarities denoted a biological kinship as manifested by reciprocal immunity. Manwell,[69] working with *P. circumflexum,* concluded that during premunition reciprocal immunity was largely influenced by strain.

The work of Hegner, Hewitt and Eskridge has further clarified the relationship between susceptibility of young red cells and the young trophozoite forms of *P. cathemerium* and other species. The relationship of developmental forms of red cells and parasites has been described,[70] and the time correlation between the degree of maturity of infected red cells and stage of parasite development determined.[71] They have demonstrated that frequency of multiple infection of red cells depends on the number and availability of young red cell forms.[72] An attempt was made to explain the affinity of young parasites for young red cell forms.[73] Parasite densities in birds were increased by experimental erythroblastosis produced by phenylhydrazine.[74]

Young[75] compared the pathological effects of different species of malaria showing *P. rouxi* to be less injurious than *P. cathemerium.*

Bloom and Taliaferro[76] described a widespread infarction in the spleen with subsequent complete regeneration following malaria infection. Splenic enlargement, infarction and compensatory hyperplasia seemed to be due largely to individual variation of the bird itself rather than to density of parasite infection.[77]

G. H. Boyd[78] concluded that survival densities of *P. cathemerium* depend both on lowering the multiplication rate (of merozoites) and direct destruction of parasites. This principle was applied on the mode of operation of the curative effect of drugs which seemed to lower the multiplication rate rather than to act directly on the destruction of the parasites.[79]

Huff[80] found no rise in the temperature in canaries infected with malaria accompanying greatest segmentation of asexual forms. Chorine[81] reported a rise in serum globulins in fowls infected with *P. gallinaceum,* due to increase of pseudoglobulins rather than euglobulins. Lion[82] found that *P. gallinaceum* had no effect on an accompanying infection of *Spirocheta gallinarum* in fowls.

Bishop[83] reported an infection of *P. relictum* in canaries for a duration of 8 years. A strain of *P. relictum* was established in pigeons by Coatney.[84] Wolfson[85] reported a strain of *P. cathemerium* in ducks, possibly suitable for experimental purposes. Coggeshall[86] reported a new species of malaria, *P. lophurae,* in the common fowl. Herman studied the epidemiology[87] and incidence[88] of avian malaria in the birds of Cape Cod. He successfully transferred infections of *P. circumflexum* to cowbirds and redwings using *Theobaldia melaneura,* and *P. cathemerium* with *Culex pipiens* and *Aedes sollicitans.*[89] Manwell[90] devised a key for classification of the avian malarias.

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THE WORK OF STATE BOARD OF HEALTH ENTOMOLOGISTS ON MALARIA CONTROL*

REPORT OF THE SUBCOMMITTEE ON ENTOMOLOGY

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During 1937, the United States Public Health Service promoted the establishment of malaria control units in the health departments of the Southern states in order that malaria control work could be undertaken in a more systematic manner. As the personnel of these units included entomologists, it was thought to be of interest to this organization to know something of the work these entomologists are doing, and the report of the Subcommittee on Entomology this year has been prepared on this subject. The report is based on information obtained by means of a questionnaire sent to the entomologists of the malaria control units. These questionnaires were also sent to officers in charge of such work in other Southern states, but the present discussion is limited to the work of the men whose primary training has been in the field of entomology and who received certain preliminary training which will be discussed herein. It should be pointed out, however, that this limitation does not mean to imply that the other states lack adequate entomological attention, as the medical and engineering personnel themselves have in many cases had special entomological training and devote considerable time to entomological work. Also some of these state

*Read before the National Malaria Committee, meeting conjointly with the Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

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authorities consult frequently with entomologists of other agencies.

Under this unit plan, entomologists were appointed by the States of Louisiana, Arkansas, Kentucky, Mississippi, Georgia, North Carolina and South Carolina. Prior to entering on their duties these men were given preliminary training in malaria and mosquito control at the laboratories of the United States Public Health Service in Savannah, Georgia, the International Health Division, Tallahassee, Florida, the United States Bureau of Entomology and Plant Quarantine, Orlando, Florida, and the Tennessee Valley Authority at Wilson Dam, Alabama. Six of the original appointees are still at work, although two and possibly a third are dividing their time with other medical problems involving insects. Only one state, Kentucky, has discontinued the work.

As might be expected, surveys to determine abundance and species of vectors and their breeding places in malarious areas constituted the chief work of these state men, an average of 50 per cent of their time being spent on this work. Their procedure in conducting these surveys follows the usual methods for establishing comparative *Anopheles* densities. These consist of locating catching stations in favorable resting or biting places in order to determine density of adults, and of "dipping" the water areas in order to establish the importance of breeding areas. The use of traps for making adult *Anopheles* collections has not come into general use. In all of the states, county employees are used as assistants in conducting surveys and a part of the entomologists' work has been the training of these assistants in their duties, and in some cases of identifying collections made by them.

The data assembled during these entomological surveys form the basis for reports to the various counties or communities on the nature of their individual problems in the control of malaria by antianopheline measures. These reports are supplemented in some cases by details of engineering features involved in the work and estimates of cost.

Research problems in connection with mosquito work occupied an average of 17 per cent of the entomologists' time. These studies were chiefly on the biology of anophelines, as for example first-brood studies and flight range. Some systematic work is being done, toxicity studies of larvicides have been made and experiments conducted on the use of vital stains for the marking of mosquitoes. A special study of the cost of malaria in one county is in progress.

Other work of these entomologists, occupying the remaining 33 per cent of their time but varying in the different states from 15 to 60 per cent, consists of educational work on malaria and mosquito control, engineering and supervisory work on WPA projects, assistance in blood-slide surveys, tick investigations and typhoid-carrier work.

To obtain information on the extent of the contact these men have with malaria control projects, an attempt was made to ascertain the number of control projects with which they are connected, the number of persons in the affected areas, and other pertinent data. Five states have given sufficient information on this point to permit analysis, although in most cases the figures given are only estimates. A total of 446 projects affecting a population of 1,635,130 were reported for the five states. Of these, 55 per cent of the projects, affecting 33 per cent of the population, involved the use of permanent measures alone, that is drainage; 20 per cent of the projects, affecting 20 per cent of the population, involved temporary measures alone, that is oiling and dusting; 22 per cent of the projects, affecting 46 per cent of the population, involved a combination of permanent and temporary measures; while only 2 per cent of the projects, affecting something over 1 per cent of the population, involved protection by screening alone.

The average population of localities protected by the various types of projects was as follows: ditching combined with temporary measures, 7,729; temporary antilarval measures alone, 3,755; ditching alone, 2,238; and screening alone, 232.

These figures seem to indicate that the size of a community has determined the nature of the antimosquito measures undertaken. The most populous communities, which of course are those best able to afford protection, have undertaken projects calling for both ditching and temporary antilarval measures. The communities next in size, averaging 3,755 persons, have undertaken anopheline control by temporary antilarval measures alone. This is rather difficult to explain, but is probably due to special conditions which may have involved impracticable drainage problems. Communities where ditching alone constitutes the antimosquito measures employed are next in order and have populations averaging 2,238 persons. In this class of com-

munities 55 per cent of the projects were undertaken, but only one-third of the population covered by the survey is included. It would appear that these localities should receive special attention by the entomologists to see whether the control being obtained is sufficient to give the desired results. If this is not the case, efforts should be directed toward instituting the necessary auxiliary measures. The population of communities where screening alone constitutes the antimosquito measure averages only 232 persons. This indicates sound procedure, as screens are the cheapest and most reliable protection for small communities in malarious regions, particularly in those where extensive swamps occur.

The Committee regrets that it has not records to present to show the reductions in adult anopheline densities which have occurred as a result of these larval control projects. It would appear from answers to our queries that, while some attention is given to "before and after" checks on mosquito density, there is altogether too little of this work being done. There is certainly a need for the collection and presentation of this sort of data, as it is often difficult to translate miles of ditching or acres drained in a given community into the actual mosquito reduction obtained. The task of working up the available records on this subject and of securing this information in a uniform manner in connection with all new projects should be made one of the essential duties of the entomological staff in each state, because reduction of adult mosquitoes at the points where protection is desired is the only criterion by which we can judge the efficacy of larval control work.

MALARIA CONTROL ACTIVITIES*

REPORT OF THE SUBCOMMITTEE ON MALARIA PREVENTION ACTIVITIES, 1939, TO NATIONAL MALARIA COMMITTEE

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State Health Department Malaria Control Operations in General.—At the present time all of the sixteen states regarded as within the malaria belt of the United States have complete units or designated personnel in the state organization through which malaria control programs are planned and initiated. This has resulted from a realization that the type of entomological and engineering survey necessary to delineate malaria foci cannot be adequately carried out as a part of a well rounded program of a county health organization. While the form of this organization varies in the several states, in at least twelve of these the malaria control unit is built around a nucleus of a medical malariologist, an entomologist, and an engineer. In some states, it is still felt that spleen examination is more feasible than thick films for determining the location of malaria foci.

Recently the Social Security allotment to the states has been increased and it was suggested that malaria, among certain other diseases, be given added consideration. This has resulted in materially strengthening the malaria control organization in many states by the addition of personnel to the centralized unit.

The activities of the centralized units have very clearly shown the advantage and value of attacking the malaria problem by definite planning through medical, entomological, and engineering surveys. By this method the endemic foci of malaria are located, the breeding places of the mosquito vector found, and definite plans with costs outlined for elimination programs following whatever means are found to be most feasible. This is a logical approach which offers definite cost data for the consideration of governmental and civic bodies or other interested groups.

Surveys.—Within the past year there has been a great increase in the number of blood slides taken and examined in state and local laboratories as a means of studying malaria distribution. To a limited degree spleen surveys have also been made for a similar purpose. State and local units have been unusually active in most of the malarious states, studying problems connected with fresh water swamps, distribution of anopheline vectors, mapping and estimating for future work, and the many usual factors encountered in the prosecution of field activities. In one state, a standardized county mapping procedure was developed last year which is now considered necessary to organized malaria control activities.

For years routine surveys have been made in many states in an endeavor to interest new urban centers to undertake malaria and mosquito control by means of seasonal larvicidal campaigns. This work has not been neglected during the past year. During the season just passed malaria

*Read before the National Malaria Committee, meeting conjointly with the Southern Medical Associaton, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

cases have appeared in some of the more northern states of the Mississippi Valley and some study has been made of conditions which might favor malaria transmission in these areas.

Education.—A very important part of any health program is that of educating the people to the need for the work. The usual talks, exhibits, motion picture shows and lectures on malaria and its prevention have been largely revised, expanded, and presented in a more effective manner through the efforts of the centralized control units and their local representatives. The publications on malaria and mosquitoes in many states have been completely revised to bring them up to date. In at least one state it has been found advantageous to give periodical talks to WPA surpervisors of malaria control drainage in order to increase their interest in the work.

Laboratory.—As mentioned earlier, there has been a large increase in the use of laboratory facilities for thick film work. In one eastern state approximately 24,000 blood slides were taken in four counties in a study of malaria distribution. In a south central state, 25,500 slides were handled for a similar purpose. In one state carrier detection and treatment has been featured, and in several states entomological studies have been carried on continuously in order to add further to the knowledge of mosquitoes and their habits.

Impounded Waters.—The disastrous effect from malaria which may follow impoundings are not overlooked. Practically all of the states in the more highly malarious regions have already adopted and put into operation strict regulations governing the creation and maintenance of impounded waters. In one state a successful effort is being made to obtain voluntary compliance from the owners of impounded lakes created prior to the adoption of impounded water regulations. The War Department in their program of building flood control reservoirs is cooperating with the state health authorities. In connection with these projects many problems occasioned by unusual conditions are being investigated. There has been little legislation concerning impounded waters from a malaria control standpoint during the year and legal safeguards seem to be fairly adequate. Paris green larvicides and oil have been used extensively on impounded waters during the year in many sections.

Maintenance of Drainage Systems.—The question of maintenance of drainage systems is one of prime importance. There have been great strides made in the design and application of permanent linings of concrete or brick for malaria control ditches. Many of the states are featuring permanent linings for town drainage. Practically all of the states where malaria is widespread are installing some form of permanent lining wherever concentrations of population will warrant the added cost. These linings are usually limited to a small invert in the ditch bottom, and this has naturally led to studies of sodding or other means of stabilizing the banks as well as modified engineering practices.

The Work Projects Administration gives favorable consideration to projects involving permanent linings and this has been a large factor in promoting this type of work. In at least two states tiling and the so-called French drains have been placed under the ditch bottom to cut maintenance cost and are proving very effective in preventing accumulation of water even where the ditch itself is allowed to become potholed.

Permanent linings have not yet been developed to the point where they are universally applicable, and open earth ditches still have their place in many areas, particularly in rural sections.

WPA Malaria Control Drainage.—This work has been continued on a basis similar to that of last year. The Public Health Service in its capacity of a reviewing and recommending agency to the Work Projects Administration is calling for more definite information on these projects through which it can make more accurate evaluation of their malaria control value. This has been necessary in view of the fact that these projects are now concerned with larger water areas than formerly and often other governmental agencies and interests are involved. It has again been necessary through reduced appropriations to further curtail the technical supervisory personnel paid by the Service to a point where it is distinctly inadequate to supervise the work properly.

The WPA malaria control drainage is being critically observed by other agencies that have interests in the larger areas proposed for drainage and it is becoming increasingly important that areas proposed for drainage be very care-

fully selected after due consideration of all the interests involved.

Screening.—During the past year, screening and mosquito proofing programs have been carried out in at least four states. In two of these the programs have been cooperative ones, either in connection with a specific problem or as a study. In a third state, National Youth Administration labor was used in mosquito proofing operations. While screening has its place under certain conditions, it is not being utilized as a routine method of malaria control.

Drugs and Their Use.—One state reported last year a program of carrier detection and drug treatment. This has been continued this year.

In one Southern state, prophylactic studies have been carried out with "atebrin" in one county and quinine in another. It is hoped this study will be continued for several seasons to come, in view of the probability of a rising malaria rate. In another state, a two-year study of the efficacy of "atebrin" was brought to a close in 1938. It was reported that a good reduction over the two-year period was shown by blood indexes. Mass treatments for the control of malaria outbreaks are reported for some special areas. One state reported that plantation owners undertook prophylactic and treatment programs on their own lands. Distribution of antimalaria drugs was carried out in five counties of an eastern state.

Legislation.—The only legislation of importance reported as bearing on malaria is from a state where the legislature passed an act calling for a state referendum to permit the people of one county to express themselves by districts on special taxation for malaria control.

Training of Personnel.—In most states the local personnel, both medical and sanitary, are now given special training in prevention activities before being assigned to the field. In view of the rapidly expanding use of thick films for malaria study purposes, several states have held training schools for laboratory technicians. The Public Health Service has assisted in this work.

Research Activities.—Although the main function of the state health department is to apply knowledge gained through outside research organizations, the state health departments give some attention to research on special problems. This research covers malarial therapy, anopheline surveys, entomological studies, larvicides, ditch linings, drug prophylaxis, and other lines of special importance.

International Health Board of the Rockefeller Foundation.—The International Health Division of the Rockefeller Foundation has continued its serologic and chemotherapeutic investigations reported on last year.

Other related studies include: (1) a specific complement-fixation test diagnostic in humans with latent malaria and negative blood smears; (2) a demonstration of protective antibodies in humans following *P. knowlesi* malaria; (3) preservation of viable malaria parasites at low temperatures; (4) studies of the invasion of the red cells by the malaria parasites; (5) the histopathology of the spleen in avian malaria. Investigations were continued on the genetics of the mosquito host and of malaria parasites in an attempt to throw light on the susceptibility or nonsusceptibility of certain mosquitoes to certain parasites.

In connection with an experimental control program in one county, antimalaria drainage in which precast cement inverts are used as a permanent lining is being studied. In this same county, the development of a practical screening program for promotion by county health departments is being attempted.

Tennessee Valley Authority.—In addition to the routine malaria control operations carried on around the lakes under the Authority's direction, studies have been made of larvicides and herbicides, and reservoir clearing prior to and subsequent to impoundage. Shade studies, hibernation studies of anopheles, and many related investigations have been inaugurated or continued during the year. A study was commenced during the year in an attempt to more closely coordinate mosquito control and wild life interests on the TVA lakes. This study is being made by representatives of all interested agencies and it is believed that the observations made will result in a better understanding and appreciation of the various interests involved. This study will probably cover several seasons.

United States Public Health Service.—The United States Public Health Service has continued its researches of malaria control by the use of drugs, malaria therapy of paresis, immunization to malaria, bird malaria, and studies of *A. walkeri.* Studies of ditch maintenance by means of permanent linings are still in progress and, while these are far from complete, yet as a result many miles of permanent linings have been installed in connection with WPA malaria

control drainage projects. A reclassification of the Anopheles of the Caribbean and Costa Rican areas is nearing completion. Investigation has indicated that characteristic desmids found in potential Anopheles producing waters may be used as a measure of anopheline production and this fact appears to open up a new field of study in connection with survey activities.

The investigations relative to the disinsectization of airplanes reported last year have been brought to a close with the demonstration and adoption of more suitable routine methods of applying larvicides for disinsectization purposes. This activity was undertaken to prevent the introduction of *Aedes aegypti* and other disease-carrying mosquitoes from abroad.

MALARIA MORTALITY IN THE SOUTHERN UNITED STATES FOR THE YEAR 1938*

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INTRODUCTION

Malaria mortality in the Southern United States for the year 1938 was on the whole the lowest on record for the area. The average rate of 5.8 per 100,000 population compares with 6.9 for the previous year, 6.6 for the low of the previous cycle (1931), and the average highs of 11.9 for 1929 and 11.4 for 1933. Nine of the fourteen states showed an improvement and five a slight regression. The most marked decline in the rate occurred in Georgia, where the 1938 rate (4.6) was approximately 40 per cent lower than the 1937 rate (7.6). The states in which there was a higher rate for 1938 than for 1937 (Alabama, 8.3 vs. 7.9; Kentucky, 1.2 vs. 1.0; Louisiana, 8.9 vs. 8.5; Oklahoma, 3.5 vs. 3.4; and Tennessee, 4.1 vs. 3.7), together with the other nine states, all had a significant decline in the 1937 rate compared with that of 1936. Thus, there is suggestive evidence that the low place in the five-to-seven year cycle has been reached, and that, barring effective man-made control, a rise in the curve is again imminent.

*Read before the National Malaria Committee, meeting conjointly with the Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

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Table 1

MALARIA MORTALITY BY STATES AND COUNTIES

State	Number of Counties	(A) 1938 Rates by Counties				(B) 1938 vs. 1937 Rates by Counties				(C) 1929-1938 Ten-Year Rate by Counties			
		Per Cent with Rate 50 or Above	Per Cent with Rate 25 to 49.9	Per Cent with Rate Under 25	Per Cent Negative	Per Cent with Increased Rate	Per Cent with Decreased Rate	Per Cent with Stationary Rate	Per Cent Negative Both Years	Per Cent with Average Rate 50 or Above	Per Cent with Average Rate 25 to 49.9	Per Cent with Average Rate Under 25	Per Cent Negative for 10 Years
Alabama	67	1.5	9.0	68.7	20.9	34.3	47.7	7.5	9.0		9.0	91.0	
Arkansas	75	2.7	26.7	52.0	18.7	41.3	38.7	8.0	9.3	13.3	30.7	56.0	
Florida	67	10.4	13.4	49.3	26.9	35.8	37.3	11.9	14.9	28.4	16.4	53.7	1.5
Georgia	159		3.1	43.4	53.5	17.0	33.3	10.1	39.6	7.5	20.7	63.5	8.2
Kentucky	120		0.8	17.5	81.7	11.7	14.2	5.0	69.1		0.8	57.5	41.7
Louisiana	64		9.4	70.3	20.3	37.5	32.8	20.3	9.4		17.2	82.8	
Mississippi	82	1.2	9.8	64.6	24.4	40.2	46.3	7.3	6.1	2.4	18.3	79.3	
Missouri	114		3.5	18.4	78.1	13.2	14.9	2.6	69.3	3.5	1.8	65.4	28.9
N. Carolina	100		2.0	34.0	64.0	18.0	23.0	8.0	51.0			71.0	29.0
Oklahoma	77		1.3	38.8	59.7	19.5	32.5	7.8	40.3		2.6	84.4	13.0
S. Carolina	46	10.9	10.9	47.8	30.4	19.6	47.8	15.2	17.4	17.4	8.7	71.7	2.2
Tennessee	95		2.1	30.5	67.4	17.9	14.7	9.5	57.9		4.2	73.7	22.2
Texas	253	0.4	0.8	27.7	71.1	11.1	23.3	4.3	61.3		3.6	62.8	33.6
Virginia	100			2.0	98.0	1.0	7.0		92.0			34.0	66.0
Total	1419	1.2	5.0	36.2	57.6	19.7	26.9	7.4	45.9	3.9	8.5	65.8	21.8

ANALYSIS BY COUNTIES AND GROUPS OF COUNTIES

A summarized comparison of important data by counties is presented in *Table 1*. In this table there are three groups of calculations. The first (A) includes the percentage of counties in each state with a 1938 malaria death rate of 50 or above, the percentage having 25 to 49.9, the percentage under 25, and those counties with no reported malaria mortality. The second (B) provides a percentage comparison between 1938 and 1937 data, indicating the percentage increased, the percentage decreased, the percentage essentially the same and the percentage without deaths for both years. The third (C) gives the 1929-1938 percentage averages for the same categories as are included under (A). It will be noted that in Arkansas, Louisiana, and Tennessee a higher percentage of counties had rate increases than had decreases between 1937 and 1938. In Louisiana and Tennessee this is correlated with the increase in the state rate. In Arkansas, where there was a slight decrease in the state rate, the figures suggest more widespread endemic malaria coupled with marked decrease in highly endemic foci. In Kentucky, Oklahoma and Texas the reverse is the case, sug-

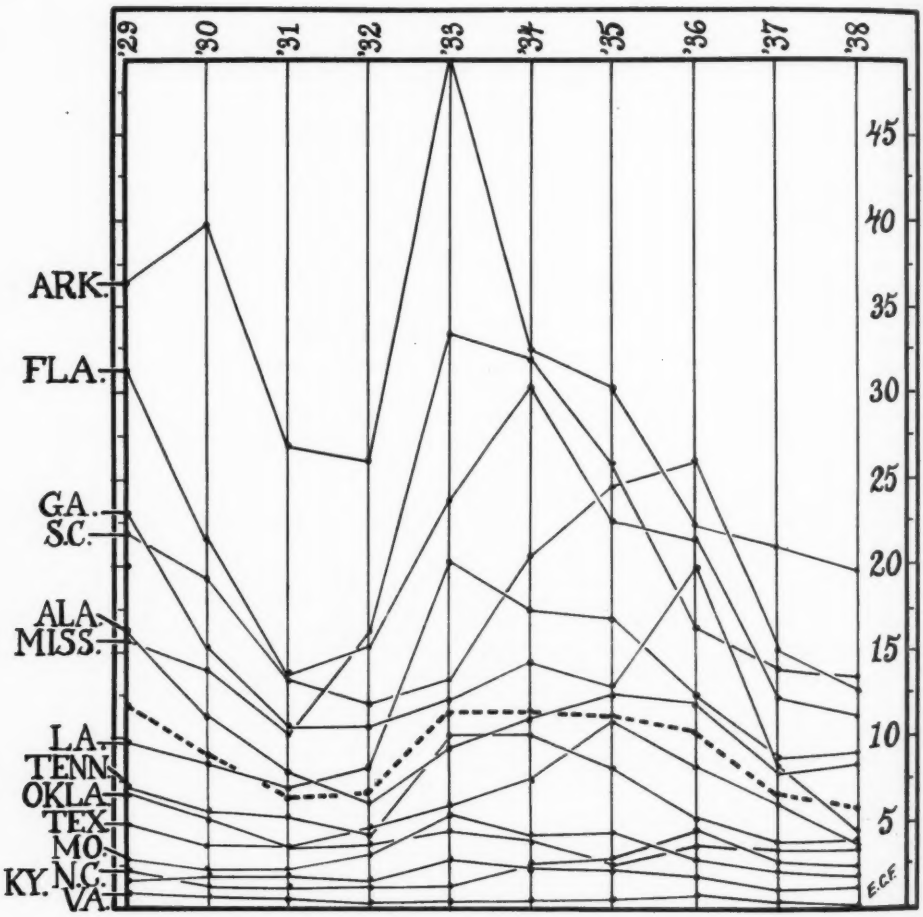

Fig. 1

Malaria mortality curves by states for fourteen Southern states for the period 1929-1938. The figures in the vertical column indicate the rate per 100,000 population, based on the United States 1930 census. The broken line indicates the average rate for all fourteen states.

gesting the reduction in malaria deaths in these states as a whole, but significant increases in special districts.

The ten-year averages will be referred to later.

MALARIA TRENDS FOR THE PERIOD 1929-1938

The average malaria mortality curves by states are presented in *Fig. 1*. This diagram shows the more or less cyclical rise and fall of the rates, with the average low of the curves in 1931 and 1938. In 1931 three states showed a slight increase over 1930, although the South as a whole did not experience a significant increase until 1933. It is noteworthy that the immediately previous highs for Georgia and South Carolina were not reached until 1936 and that these two states had precipitate declines in the following two years.

Analysis of the 1929-1938 period by counties (see *Table 1*) shows an average high malaria mortality (50 or above) in 28.4 per cent of the counties of Florida, 17.4 per cent of the counties of South Carolina, 13.3 per cent of the counties of Arkansas, 7.5 per cent of the counties of Georgia, 3.5 per cent of the counties of Missouri, and 2.4 per cent of the counties of Mississippi. In none of the other states did a single county have an average rate as high as 50. The localization of highly endemic malaria in rather restricted foci is indicated by the fact that, with the exception of the areas of moderately high endemicity in the Red River Valley and the lower Rio Grande, practically all of the highly malarious territory is confined to the southeastern wedge of counties and to the Cairo-Natchez portion of the Mississippi Valley. Nevertheless, except for the southern Appalachian highlands, practically all of the remaining counties of the South are found to be malarious. These statements are better appreciated when the average 1929-1938 rates are presented in the form of a map (*Fig. 2*). It is believed that this map is a more accurate representation of malaria in our area than the maps previously published by Maxcy[1] for 1919-1921, by Dauer and Faust[2] for 1929-1933 and by Faust[3] for 1933-1937. While the main features of these previous maps are similar to those for the 10-year period, the temporary high rates of one or two years are equalized by lower rates over other years. Similarly many counties, which would appear to be free of malaria deaths for a particular year or small group of years, are found to have had one or more deaths when a decennium is reviewed.

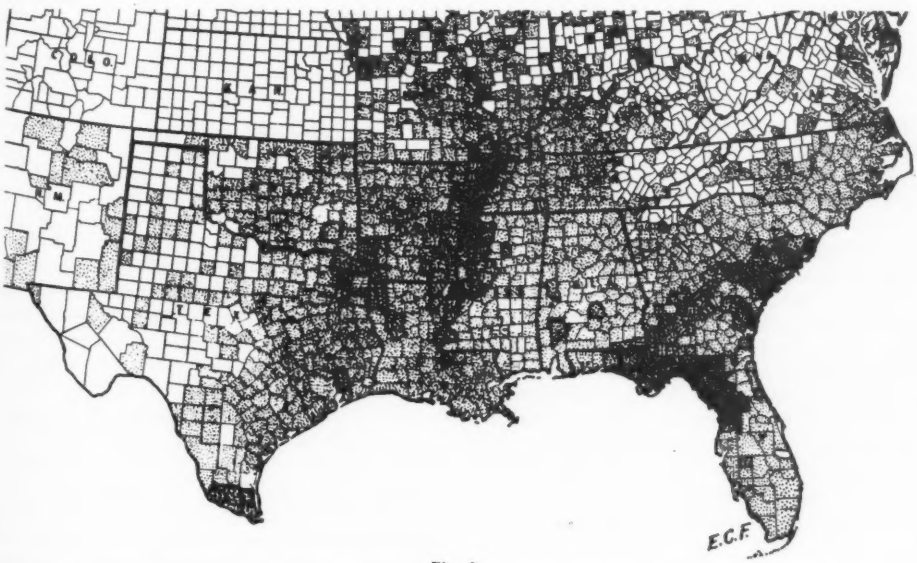

Fig. 2

Malaria mortality by counties in the Southern United States for the decade 1929-1938. The black areas indicate an average rate of 50 or more per 100,000 population for the 10-year period; the heavily stippled areas, an average rate of 25 to 49.9; the lightly stippled areas, a rate below 25; the unshaded areas, no reported malaria deaths for the decade. (Compiled from annual reports furnished Dr. Faust by the bureaus of vital statistics of the several state departments of health.)

This brief evaluation of malaria mortality is presented in order that the 1938 rates by states and counties, together with comparisons with previous years of the past 10-year period, may be recorded.

SUMMARY

The summarized death rates by states and by counties in the Southern United States for 1938 have been presented. These rates have been compared with those for 1937 and for the period 1929-1938 in order that the trends in malaria mortality may be noted. The average rates for the 1929-1938 period have been calculated by counties and have been plotted on a map in order that the highly endemic foci and the general distribution of the infection in the Southern United States may be better visualized.

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ENGINEERING PHASES OF MALARIA CONTROL*

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Since the Chairmanship of the National Malaria Committee has been entrusted this year to an engineer, I take the liberty of addressing this Committee on engineering phases of malaria control. I personally feel very deeply the public health engineer's responsibility for prevention of malaria.

I desire to take this opportunity to pay tribute to those of other professions who have abundantly contributed to malaria prevention. I wish to make particular reference to those early medical scientists who by personal sacrifice made discoveries on the cause of malaria. This has enabled the engineer to contribute materially to malaria control by the application of engineering in various phases.

Let it not be inferred that I am placing a restricted definition on engineering. Engineering has a very broad application to all phases of public health. Therefore, for the purpose of this discussion I am including as collaborating malariologists those who by specialized training and experience in the basic sciences have become invaluable as collaborators in malaria engineering. Then I briefly summarize conclusions that in evaluation of any malaria control program we necessarily consider medicine, engineering, biology, chemistry, entomology, economics, and other sciences. Should we not include these we may fail to grasp the true perspective of effective malaria control.

In presenting the subject of engineering phases of malaria control it may be in order to define engineering and its specific application to this subject. Engineering may be defined as the art of directing the forces of nature to the benefit of man by control of environment. Then necessarily malaria engineering is the art of directing the forces of nature to the benefit of man by control of those forces which influence malaria. I am convinced that by training and experience public health engineers are so qualified, especially those whom I know as members of this National Malaria Committee.

After this period of scientific discoveries by the medical and other professions, there necessarily followed development of practical engineering methods to remove the cause and thereby prevent malaria. We who follow public health in all of its phases subscribe to a common philosophy, that is: the cause of any disease must be thoroughly understood before we can technically establish means for prevention. Also we generously give credence to that old maxim "an ounce of prevention is worth a pound of cure." Then by knowing the cause of the disease we can effect prevention by engineering methods in so directing the forces of nature. In so doing we take into consideration many phases of engineering. Drainage is probably the most prominent, although there are many other engineering phases.

It is evident that the engineer, by reason of his professional training and experience, is necessarily concerned with and is responsible for consideration of, first, the economic loss involved by the prevalence of malaria; second, the engineering and economics of control methods; and third, the engineering feasibility of accomplishing the objective. The engineer should seriously consider the initial cost of malaria control as well as annual maintenance. He should

*Chairman's Address, National Malaria Committee, meeting conjointly with the Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

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consider if the project is a sound financial investment based upon the local health and economic benefits to be derived. He may find that engineering methods cannot be practically applied. Then he should consider other methods.

One of the prerequisites for a well qualified malaria engineer is a satisfactory record of engineering experience and of engineering accomplishments in both planning and construction. This brings up the question of the value of the engineer in his ability technically to analyze and clearly to present a comprehensive engineering report relative to the specific problem.

There are three very important essentials relative to any malaria engineering project. These three essentials may be listed in order of importance: first, a comprehensive engineering report stating the public health problem involved and denoting its social importance; second, complete and comprehensive engineering plans and specifications showing engineering feasibility; and third, an estimate of initial cost, also annual maintenance cost; and finally the methods of financing. The report should be developed from engineering facts and the public health objectives should be very specific. The engineering report should be supplemental to a medical, epidemiologic and biological report. If this latter service is not available, then the engineer should be so qualified that in the absence of this service he can prepare the complete report. It is essential, therefore, that the malaria engineer have a practical knowledge of such correlated essentials as epidemiology, biology, parasitology, and other such phases of malaria control.

It may be appropriate to present a hypothetical case of the role of the engineer in a community where an engineering malaria control project is necessary.

The physicians have experienced an unusual number of calls from a community. The cases have been diagnosed as malaria. The problem has been reported to the state health department and assistance requested. The state epidemiologist or state malariologist, as the case may be, visits the community and makes a preliminary investigation. The problem is considered sufficiently important to warrant a planned program for malaria control. However, nothing is known of geography, topography, hydrology, biology, entomology or economics. There is nothing concrete as a basis upon which to proceed except the prevalence of malaria. Before an intelligent analysis can be made it is quite evident that the first requisite is an accurate map of the entire community. The engineer is called upon to prepare the necessary map. Emphasis is placed on necessity for an accurate map. There is no place in engineering technic for misrepresentation in the form of a sketch. We may define mapping as the art of finding the peculiar features, elevations, contours, dimensions and positions on a portion of the earth's surface and accurately representing on paper the information found. The technically drawn representation is called a map. On this map, then, may be accurately shown all places of human habitat as well as places of insect habitat. The map may be then used for epidemiology by indicating foci of malaria infection found by blood or spleen index or by both. It is further used for biological and for entomological data and for such indications as may be appropriate with reference to hydrological features. It then becomes indispensable to the engineer and others as a basis for planned malaria control. He then proceeds generally with plans which involve elevations, profile grades, cross-sections, and so on. I emphasize that for all features relative to malaria control the map is the first requisite and is fundamental for intelligent and effective planning. When the map has been completed and all necessary investigations made and recorded it is coordinated for a comprehensive report presenting epidemiology, engineering, biology and economics. We should then feel confident of a job well done by the application of engineering to malaria control.

It is quite evident that there are many malaria engineering projects planned and executed at unwarranted cost even though the health problem may be acute. Whereas it is true that we cannot afford to have malaria, it is also true that malaria control involving expensive engineering methods often cannot be afforded. In such a case there is evidently some other solution to the problem. Therefore, the engineer should carefully analyze the problem and consider the efficacy of other methods which may be economically justified under the peculiar circumstances. By this he may demonstrate his resourcefulness.

One who has had specialized experience in engineering phases of industrial evaluation necessarily possesses a valuable qualification for malaria engineering. Such an engineer could take stock of assets and liabilities and place these in balance with the economic and social need for malaria control before the investment is recom-

mended. The need for this in malaria engineering is quite evident. The engineer by training and experience should be best qualified to deal with the economics of the problem. We who are engaged in this phase of public health know from experience that generally the end justifies the means and that malaria control will pay exceptionally high dividends. Reference may be made to some of these instances. Some years ago an industrial camp manager of a well-known corporation made this statement:

"By means of malaria control and sanitation we have obtained more working days per man, more stability, less sickness in camp, and in a three-year period the average increase of earning per man-month has been from $30.79 to $40.00."

This is practically a 33 per cent increase in labor output. One large sawmill and box factory in the South stated that minor drainage operations near its plant in 1915 and 1916 were worth $35,000 per year to the company. An antimalaria campaign in one Southern state made it possible for a lumber company to ship 20 per cent more lumber and this increased the revenue of the railroad company by $30,000 per year. If malaria control has been of such benefit to industry, it is quite evident that a well-planned and executed malaria control program will be of equal economic benefit to individual families in a community.

Malaria control costs money and those who hold the purse strings are generally cold to humanitarian appeal. Many such individuals are more parsimonious than humane. Consequently, it becomes necessary for the engineer to be prepared to present the problem to the public in terms of what may be expected in economic profit.

I take this opportunity to refer to a somewhat new phase of engineering which evidently will be of considerable value in future state malaria control. I have reference to recent initiation of modern governmental methods of agricultural engineering. I have been impressed with its possibilities as an asset to state-wide malaria control operations. I do not have reference to agricultural drainage to which we often refer as land reclamation. I have in mind methods such as soil erosion prevention through means of terracing, reforestation, seasonal cover crops, and contour strips of leguminous crops for soil holding and enrichment, all of which have a tendency to prevent soil erosion. Many of you have evidently observed in your states the influence of rapid rainfall run-off, resulting in soil erosion to the detriment of streams and lowland areas. The effect has been the irretrievable loss of tons of fertile soil as well as retention of the flow of streams. The result has been the flooding of meadows and swamps and development of quadrimaculatus producing areas. We know very little of the original conditions of field and forest previous to the advent of cotton cultivation. We know very little of the original conditions of our streams previous to certain abuses by man as he became a tiller of the soil. Man in those days little realized that he was guilty of robbing and plundering and that some day posterity would necessarily pay the penalty. If man in those days saw clear crystal streams in pristine purity winding down through primeval forests and green pastures, little did he appreciate Mother Nature's great endowment. He was only enamored by the fertility of the soil on the hills and took no thought for the morrow as to the value of soil conservation. He did not visualize the future when man's health would be jeopardized by his greed for the soil. We now have a public health problem because of soil erosion.

The problem to which I refer is not so generally existent in the Coastal Plains of our Southern states as in the Piedmont Plateau sections. I am familiar with numerous conditions of this kind in our State which have in recent years been responsible for malaria epidemics. It may be of interest to you that in one particular county of our State we have been urged to make plans and estimates on a stream for malaria control by drainage. This was a typical soil erosion problem and malaria was prevalent. We realized the inevitable excessive initial cost and also the impracticability of maintenance under the circumstances. We called a public hearing and emphasized the importance of soil erosion prevention by various means. We suggested that drainage improvements be deferred and considered only as secondary measures to soil erosion prevention. We stressed the need for reforestation, cover crops and terracing. Possibly this was considered a somewhat radical departure from usual theory and practice of malaria engineering. We did, however, suggest such methods as screening and treatment by drugs as immediate measures. We considered this a drainage engineering problem not worthy of the

estimated cost due to anticipated rapid silting and overflow. We concluded that drainage would be advantageous only after other conditions were made satisfactory for drainage maintenance. Also it was logical to assume that subsequent to agricultural engineering by prevention of soil erosion there would result a higher standard of living and that this alone would influence some reduction of malaria. We who have observed malaria in its many phases know that raising the standard of living will probably decrease the prevalence of malaria. Also that an already impoverished community cannot afford to spend money beyond the expectation of a profitable investment. Let it not be inferred, however, that we minimize the value of drainage. We continue to give drainage first place among methods of malaria control.

Again I refer to the definition of engineering as the art of directing the forces of nature to control of the environment. How many of us have a true perspective of the common rural environment? The environment as we find it locally represents the standard of living for that particular community. While we are so absorbed in research, investigation and engineering phases, let us pause to consider with sympathetic understanding this phase of the lower standard of living and its effect upon the public health.

When we analyze the standard of living we find the greater prevalence of malaria and other diseases where the standard of living is lowest. The problem is one for the sanitary engineer and for the malaria engineer. It is true that especially under new governmental trends we have made a start on improvement of rural living conditions, but not in comparison with progress on urban slum clearance. Slum clearance in the cities by Federal expenditure is in greater proportion than expenditures for rural housing. However, at least three of the Federal agencies are active in improving the rural standard of living. I can say that at least in our State these Federal agencies are cooperating with the State Department of Health in elevating the rural standard of living and we may anticipate its influence in a reduction of malaria.

It may be of interest to refer to a survey of our State made in 1934 which indicated the low standard of living in our rural communities. This survey showed that of all the farm homes, 16 per cent had no toilets whatsoever, only 1 per cent had bathtubs and bathroom plumbing, 83 per cent had outdoor toilets, 93 per cent of which were a menace to public health, and only 2.5 per cent had kitchen sinks. Seventy-nine per cent of the houses were unpainted, and 43 per cent had defective roofs. Figures were not given relative to screened homes, but I would venture to estimate that only 1 per cent or less had screening in order to protect occupants against malaria. It is true we have made progress in rural home sanitation since 1934 and our public health statistics so indicate. It is evident, however, that we must have some control of the standard of rural living before we can have the most effective control of malaria. It seems logical to believe that eventually every county health department, especially in Southern states, will have some control of the plans and specifications of rural residences. This could be accomplished by approval of all plans and specifications by the county health department for health protection such as water supply, sewerage, and malaria prevention by mosquito proofing of houses. Most of our cities have building restrictions enforced by municipal building inspectors. If it is advantageous in the city, why should it not be advantageous in the country? This problem represents only another engineering phase of malaria control. Therefore, I present for consideration of malaria engineers this question of better housing for improving the standard of living. Let us be ever alert to discover new engineering phases lest we retrogress rather than progress. Let us continue as pioneers in this field of malaria control always alert to discover new and more effective methods.

In discussing engineering phases of malaria we may by grammatical transposition reverse our subject and discuss malaria phases of engineering. We regret to admit that the engineer has often been responsible for the cause of malaria by either ignorance or indifference to malaria phases of engineering. However, most of this antedates early railroad and highway construction. Engineering is probably not the only profession responsible for this gross error. It is common knowledge that in the tropics in those early days of yellow fever pans of water were placed under hospital bed posts in order to protect the patient from crawling insects. This made conditions conducive to production of yellow fever mosquitoes in the hospital wards. Just so the engineer in construction of railroads and

highways created borrow pits for obtaining earth for filling, little realizing that in so doing he was inducing production of malaria mosquitoes. Many malariologists are today making reparations and no one is doing more than the engineer to correct these early errors. Malaria engineers are constantly filling and draining borrow pits and influencing civil engineers not to create new ones. Engineers continue designing hydroelectric plants, necessitating creation of large bodies of water. It is gratifying that the hydroelectric engineer is conforming to state standards on these impounded areas in order to prevent malaria, all of which indicates that the engineer of today is seriously considering malaria phases of engineering.

In further consideration of engineering phases of malaria control, it may be appropriate to refer to the present international situation. Let us direct our thoughts to malaria in times of war. We have only too often heard the malariologist eloquently resort to that common and popular phraseology, "Malaria has been the cause of the loss of battles and the fall of nations." This may be true, or it may not, but we do know the value of malaria control in times of war. Should this country become involved in war it would be necessary to mobilize a large army within a short period. It would be necessary to select cantonment sites and protect our soldiers against the ravages of malaria. Sanitary engineers well know that it often takes years to perfect sanitation in a large city so that the health of the population may be protected. In time of war it may be necessary to accomplish the same purpose within a few days or weeks. Malaria prevention in Southern cantonments would involve all engineering phases of malaria control. This is something we do not anticipate, but all engineers engaged in public health work should be prepared to meet such eventuality. The National Malaria Committee should then promptly serve as a scientific organization coordinating its knowledge and resources for assisting in prevention of malaria in army cantonments. We have faith that malaria engineers would meet this responsibility with distinction.

Southern Medical Journal
JOURNAL OF THE
SOUTHERN MEDICAL ASSOCIATION

Copyright, Southern Medical Association, 1940. Published monthly by the Southern Medical Association, Empire Building, Birmingham, Alabama. Annual subscription, $4.00. Single copies, 35c each.

Entered as second-class matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

M. Y. DABNEY, M.D., Editor
C. P. LORANZ, Secretary, Treasurer and General Manager

Volume 33 AUGUST 1940 Number 8

EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
Thirty-Fourth Annual Meeting
Louisville, Kentucky, November 12-15, 1940

HEARTS OF THE WELL-TO-DO MIDDLE AGED

Rather important in preventive health work in America are the life insurance companies, which profit by extending the life span of the assured. In this work buyer and seller, that is, company and policyholder, usually cooperate in harmony. Their aims are identical.

Largely through insurance statistics has it been established that overweight is a menace to longevity, and that diabetes, for example, is more common in the overweight than in the underweight.

The Life Extension Examiners[1] have recently published results of a study of the electrocardiograms of a group of 2,400 presumably normal men who were maintaining insurance policies of more than $25,000. The policyholders came from all parts of the country, and were both urban and rural. Their average age was 47.8 years.

They were classified according to the electrocardiograms in three groups: (1) normal, (2) with borderline changes, and (3) as showing definite impairment of the heart. Definite impairments were such changes as a "PR interval of more than 0.21 second; QRS interval more than 0.11 second; inverted or diphasic T_1; inverted or diphasic T_2; relatively deep Q_3; auricular fibrillation, or any combination of these." Only about one in three of the assured was classified as clearly normal. More than half came in the second or borderline group, and one in ten had definite impairment.

About nine out of ten of those with definite impairment as shown by the electrocardiogram had no symptomatic complaint. They had come for study only because their policy permitted a periodic health examination. About half of the last two groups were overweight. Group 1, with no suggestion of abnormality in the electrocardiogram, contained a large number of underweight persons.

Enlargement of the heart occurred in nine out of ten persons of Group 3. Systolic murmurs occurred twice as frequently in Group 3 as in Group 1. Systolic blood pressure of more than 150 occurred in around 20 per cent of Group 3, and about 3 per cent of Group 1. Diastolic pressure of more than 100 was detected in 2 per cent of Group 1 and in nearly 15 per cent of Group 3. Abnormal electrocardiograms were much more common among smokers than among non-smokers. This might be considered as a toxic effect of nicotine. However, it is possible that non-smokers as a group are more abstemious or temperate in their food and general habits.

Such studies as these are most informative and serve to emphasize the importance of the periodic health examination of well persons, and the value of including an electrocardiogram in the study when this can be done. Since a considerable number of the impaired showed no symptoms, one may say that clinically the conditions were probably not diagnosable.

The work is also of value in demonstrating what may be expected from the hearts of a group of men under 50 in easy circumstances and presumably normal at the time of taking out a large insurance policy.

1. Johnson, H. J.: A Study of 2,400 Electrocardiograms of Apparently Healthy Males. J.A.M.A., **114**:561-3 (Feb. 17) 1940.

THYROID AND SHOCK

Attempts have been made to combat shock in various ways, one being by injections of adrenal cortical extract. A dependable method of producing shock in dogs, according to Schachter and Huntington,[1] of the University of Chicago, is by feeding the animals desiccated thyroid for a

1. Schachter, R. J.; and Huntington, J.: Use of Orally Administered Desiccated Thyroid in Production of Traumatic Shock. Proc. Soc. Exper. Biol. & Med., **44**:66 (May) 1940.

week before trauma is used. The amount of thyroid administered was about sufficient to raise the basal metabolic rate 20 per cent. Normal dogs after severe trauma to the limbs and testicles and prolonged manipulation of the intestines, fail to go into shock in eight hours. The hyperthyroid dogs responded to these injuries immediately by symptoms of shock, and the blood pressure had fallen to zero in three and a quarter hours.

The mechanism is of course of much interest. Its study may explain the development of postoperative thyroid crisis, which is akin to shock, in patients with hyperthyroidism. Information is needed about the blood potassium level in hyperthyroidism, since investigators elsewhere have shown that potassium tends to rise in the blood with increase in temperature.[1] If potassium is high in hyperthyroidism or in shock, measures to lower it might offer some symptomatic benefit.

PANTOTHENIC ACID IN B DEFICIENCY

More precise studies of the diseases arising from a deficiency of certain of the water-soluble vitamins have been made since synthetic nicotinic acid, vitamin B_1, riboflavin and vitamin B_6 have become available for clinical investigation. In a recent editorial[2] the therapeutic value of a number of the components of the vitamin B complex was discussed.

It has been shown[3] that nicotinic acid is specific for certain symptoms of pellagra; thiamin hydrochloride, for nutritional polyneuritis;[4] riboflavin, for the angular stomatitis and the ocular lesions characteristic of riboflavin deficiency;[5] and Vitamin B_6, for the muscular rigidity which sometimes follows a deficiency of this substance.

Pantothenic acid, another component of the vitamin B complex, has recently been isolated and synthesized. The first indication of its importance in human nutrition was reported by Dr. Tom D. Spies, of Birmingham, at the meeting of the Chattahoochee Valley Medical Association in Atlanta on June 10, 1940. Spies and his associates[1] have shown that the concentration of pantothenic acid in the blood of persons having pellagra, beriberi and riboflavin deficiency is from 23 to 50 per cent lower than in normal persons; that the intravenous injection of as much as 100 milligrams of either calcium pantothenate or sodium pantothenate does not produce toxic effects; that the pantothenic acid content of the blood is increased soon after injection of the crystalline material, but returns to its previous level within 24 hours; and that a simultaneous increase in the riboflavin content of the blood of persons with riboflavin deficiency occurs following the administration of pantothenic acid. These observations suggest that pantothenic acid plays a role in human nutrition and offer further evidence that deficiency diseases are mixed in nature.

In the clinical picture, symptoms of one deficiency state may predominate, but to the practicing physician this should indicate the necessity of searching for others. The earlier and more accurate the initial diagnosis, the more likely is the physician to avoid futile treatment and give specific therapy for each deficiency state present, thus saving the patient months or even years of ill health.

RIBOFLAVIN AND THE EYE

Southerners, according to the Secretary of Labor, have no shoes. Neither, according to several investigators,[2] [3] have they very good eyes, the latter because of a food deficiency, ariboflavinosis, frequently associated with pellagra. Ariboflavinosis is likely to cause comedones, shark skin complexions and sore mouth corners, as well as the eye symptoms.

In 1933 and 1934 Langston and Day[4] reported nutritional cataracts in the albino and Norwegian rat, which could be arrested by administration

1. Brewer, George: Relation of Plasma Potassium Level to Metabolic Activity. Amer. Jour. Physiol., **129**:245 (May) 1940. Editorial, Potassium and Temperature. Sou. Med. Jour., **33**:665 (June) 1940.

2. Editorial: The Onset of Human B Deficiency. Sou. Med. Jour., **33**:554 (May) 1940.

3. Spies, T. D.: The Vitamin B Deficiencies. Trans. and Studies of the College of Physicians of Philadelphia, **8**:12 (April) 1940.

4. Aring, C. D.; Evans, J. P.; and Spies, T. D.: Some Clinical Neurologic Aspects of Vitamin B Deficiencies. J.A.M.A., **113**: 2105 (Dec. 9) 1939.

5. Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M.; and Kruse, H. D.: The Ocular Manifestations of Ariboflavinosis. J.A.M.A., **114**:2437 (June 22) 1940.

1. Spies, T. D.; Stanbery, S. R.; Williams, R. J.; Jukes, T. H.; and Babcock, S. H.: Unpublished observations.

2. Spies, T. D.; Bean, W. B.; and Ashe, W. F.: Recent Advances in the Treatment of Pellagra and Associated Deficiencies. Ann. Int. Med., **12**:1830 (May) 1939.

3. Sydenstricker, V. P.; Sebrell, W. H.; and Cleckley, H. M.: The Ocular Manifestations of Ariboflavinosis: A Progress Note. J.A.M.A., **114**:2437 (June 22) 1940.

4. Langston, W. C.; and Day, P. L.: Nutritional Cataract in the Norway Rat (Mus Norwegicus). Sou. Med. Jour., **26**:128, 1933. The Arrest of Nutritional Cataract in the Albino Rat by the Use of Vitamin G (B2). Ibid., **27**:170, 1934.

of the vitamin B_2 complex. This was before the purification of any of these vitamins. More recently the effects of deficiency of the B_2 factors on the human eye have been observed.

The eye symptoms, according to Sydenstricker, Sebrell and Cleckley,[3] occur before the sore mouth corners and other signs of this particular disease appear. The earliest manifestation of ariboflavinosis is a variety of dimness of vision and photophobia, with corneal vascularization and keratitis. It was noted among a group of markedly B deficient patients, under treatment for pellagra and allied syndromes, and also among eighteen apparently well nourished institutionalized employees, provided with a presumably adequate diet, which proves how little is actually even now understood of the B requirement. Symptoms in these workers, as in the ill patients, were arrested by administration of a purified portion of the vitamin B complex, riboflavin.

What arouses particular interest in B deficiency symptoms is the fact that for this dietary factor an abundant ready made clinical material is available for study. Human B deficiency is so common that it is possible for several groups of investigators to analyze the numerous specific manifestations of the several isolated factors. The most abundant source of B deficient men, women and children apparently is provided in the population below the Mason-Dixon line.

TWENTY-FIVE YEARS AGO

From Journals of 1915

Treatment of Pellagra in the Insane Asylum at Milledgeville, Georgia.—While not recognized as pellagra until after Searcy described and pointed out the disease in 1907, the writer remembers distinctly a very fatal outbreak of this malady as early as 1905. * * * The condition was frequently captioned "foot and mouth disease" * * * due to the fact that the lesions occurred in the mouth and over the dorsal surface of the feet. * * * The death rate was high * * * the medicinal treatment has included almost everything recommended, * * * arsenicals * * * urotropin and calcium sulphide * * * salvarsan * * * cadodylate of soda. * * I am now almost sanguine that a free liberal diet should be administered in the very beginning of these cases and that the nurses should use every means to see that the patients get plenty of meat, eggs and milk.[1]

Pellagra and Parasites.—In Kentucky, the vast majority of the cases of pellagra, in fact, practically all of them, have hookworm disease or some other intestinal parasitic infection.[2]

Nails in Pellagra.—Miss W. * * * aged 29 * * * has noticed that her hands have been red and sore as if sunburned each summer for the last six years * * * heaping up of pinhead-sized horny elevations of the skin surface * * * scattered pustules over the face, becoming quite numerous on the chin * * * a white band one-eighth inch in width running across each finger nail just a little in advance of the lunula, and in each white band, sometimes at the edge, sometimes in the center, there was a crack * * * on the nails of the second, third and fourth toes of the right foot the same white transverse band is present. * * * A young man * * * had the transverse band in the middle of each finger nail. The nails were thickened, rough and irregular. * * *[3]

Pellagra and Insanity in Egypt.—In the table of "causes of insanity" pellagra is classified under "toxic agencies" * * * "the abuse of hasheesh is not the principal cause of insanity. Pellagra appears to be far more important."[4]

Pellagra and Pyorrhea.—All writers on pellagra say: The etiology is unknown. While we do not base our findings on rigidly scientific data, we have circumstantial evidence of a corroborative nature which is merely convincing that pyorrhea alveolaris is a cause.[5]

Number of Pellagra Cases.—Although Osler, in his 1907 edition of Principles and Practice of Medicine, states that pellagra has not been observed in the United States, there are today in the United States fifty thousand cases, and in some sections the death rate of pellagra exceeds that of typhoid fever.

Fly.—The fly has a distribution equal to that of pellagra, * * * the seasonal recurrences of pellagra follow closely the reappearance of the stable fly in spring. A mononucleosis in the blood of pellagrins, and long intervals of quiescence in the disease, followed by relapses, indicate a parasitic origin.[6]

Tonsillectomy.—At once and thoroughly remove all the foci. This is the vital point and is best accomplished by complete tonsillectomy. * * * If for any reason this operation is prohibited, repeated slicing of tonsils followed by the repeated curettement and expression of contents, may be resorted to and sometimes succeeds well.[7]

Autoserotherapy in Pellagra.—We were led in June, 1913, to try the effect of autoserotherapy in the treatment of pellagra. We have been perfectly satisfied with the results in each case.[8]

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1. Little, Y. A.: The Dietetic Treatment of Pellagra, with Report of Eleven Cases. Sou. Med. Jour., 8:659 (Aug.) 1915.

2. McCormack, Arthur T.: Discussion, Symposium on Pellagra. Ibid., p. 670.

3. Brownson, W. C.: An Unusual Condition of the Nails in Pellagra. Ibid., p. 673.

4. Babcock, J. W.: Pellagra in Egyptian Asylums, 1913. Ibid., p. 689.

5. Smith, D. L.; and Moore, G. Y.: Pyorrhea Alveolaris as a Cause of Pellagra. Ibid., p. 692.

6. Frayser, B. H.; and Smith, David O.: Pellagra in Panama. Ibid., p. 678.

7. Dorsey, Rufus T.: Pellagra: the Cause and the Cure. Ibid., p. 683.

8. Palmer, E. E.; and Secor, W. L.: J.A.M.A., 1915. Abst., ibid., p. 692.

Journal in New Home.—The JOURNAL is now settled in its new home, 516 Empire Building, Birmingham, Alabama.[9]

War.—Dr. Earle Drennen, of Birmingham, arranged to leave July 10 for Juilly, France, to assume charge of the Whitney Hospital, founded by Mrs. Harry Payne Whitney.[10]

9. Editorial, Ibid., p. 735.
10. Sou. Med. News, Alabama. Ibid., p. 737.

Book Reviews

Essentials of the Diagnostic Examination. By John B. Youmans, B.S., M.S., M.D., Associate Professor of Medicine and Director of Postgraduate Instruction, Vanderbilt University Medical School, Nashville, Tenn. 417 pages, illustrated. New York: The Commonwealth Fund, 1940. Cloth $3.00.

The author states in the preface that the purpose of his book is to provide an outline of examination which will help the physician to detect the common pathologic conditions. He has attempted to select those diagnostic methods which can be simply performed in any physician's office without expensive equipment and has tried to emphasize the importance to the physician of examining every patient according to a definite routine in order to avoid overlooking important manifestations of disease. The book is divided into two main parts, one of which deals with the history and physical examination and the second of which deals with laboratory methods. There is also an appendix which contains practical information concerning how to set up a laboratory in a physician's office and considers such questions as chemicals, reagents and stains. All of this material is treated in a small volume which can easily be slipped into the physician's pocket and is not more than one-half inch thick.

When allowance is made for the breadth of the field which the author covers the reader will readily realize that he has done his task superbly well. There is no waste material. Each page is full of practical information in regard to the diagnosis of disease. Although the section dealing with the physical examination covers less than 150 pages, it is remarkably complete. Beginning with a general inspection of the patient, the author gives in minute detail the important methods of examining each part of the body and mentions the various diseases in which abnormalities in a given portion are likely to be detected.

The section on laboratory methods is up to the same standard as that on physical examination. Here again only points which are of direct practical value are considered. Special emphasis is placed on urine, blood, sputum and feces. However, there is a brief but inclusive discussion of the examination of blood by chemical methods. Technics for the various important blood chemical examinations are given in detail.

This book fulfills in an excellent manner its purpose of supplying a useful practical summary of diagnostic methods for the general practitioner. The only weakness which the reviewer can find in the book is that the section on history taking is too short, although the part of it which is covered is very well done. To devote only fourteen pages to the subject of history taking in a book covering nearly 400 pages and dealing with diagnostic examination seems to place altogether too little emphasis on the history which is after all the most important method of examining the patient in the majority of diseases. However, if a physician wishes to have a book which he can keep in his bag or carry in his pocket and which contains a large amount of information in regard to the physical examination and laboratory procedures, he cannot find anywhere a better book than this one.

Clinical Parasitology. By Charles Franklin Craig, M.D., M.A., (Hon.) F.A.C.S., F.A.C.P., Col., U. S. Army (Retired), D.S.M., Emeritus Professor of Tropical Medicine in the Tulane University of Louisiana, New Orleans, Louisiana; and Ernest Carroll Faust, M.A., Ph.D., Professor of Parasitology in the Department of Tropical Medicine, Tulane University of Louisiana, New Orleans, Louisiana. Second Edition. 772 pages, illustrated. Philadelphia: Lea & Febiger, 1940. Cloth $8.50.

This is a thoroughly revised edition of the popular book, "Clinical Parasitology," by Craig and Faust. New material brings the volume up to the minute. The general introduction orients the reader to parasitology. There are three principal divisions in which are considered protozoa, helminths and orthropods. A thorough discussion is given each parasite according to its importance. Synonyms, history, geographical distribution, morphology, life cycle, epidemiology, pathology, symptomatology, prognosis, treatment and prevention are discussed. The illustrations, mostly diagrammatic, are excellent. A few actual photographs show parasites or parasitic lesions. In the back of the book is a valuable technical appendix which gives many important methods for study of parasites and parasitic disease. A voluminous bibliography lists the important references and texts on clinical parasitology.

The book is designed to meet the needs of physicians, pathologists and clinical pathologists. It gives complete information and should be a great help in recognition, diagnosis and treatment of parasitic disease. The student will find it an ideal text.

The Pathology of Internal Diseases. By William Boyd, M.D., LL.D., M.R.C.P., Ed., F.R.C.P., Lond., Dipl. Psych., F.R.S.C., Professor of Pathology and Bacteriology in the University of Toronto, Toronto. Third Edition. 874 pages, illustrated. Cloth $10.00.

This popular textbook on pathology of internal diseases is now in its third edition. From it, a complete and modern conception of the various medical diseases can be obtained readily.

The book is divided into seventeen chapters, in which are discussed diseases of the heart, arteries, respiratory system, stomach and duodenum, intestines, liver and gallbladder, pancreas, kidneys, adrenal glands, thyroid gland, parathyroid glands, pituitary body, blood, bone marrow, spleen, lymph nodes and thymus and nervous system. In general, the clinical symptoms are correlated with the pathologic lesions.

New material is presented in almost every section. Much of the book has been rewritten. The etiologic role of streptococci in rheumatic fever is rightly questioned. Under the heading "Hypertensive Heart Dis-

ease," so-called chronic myocarditis, is briefly discussed. In the section on "Diseases of the Arteries" the relation of high blood cholesterol and arteriosclerosis is discussed. Although there is lack of proof of a direct relation of cholesteremia and atheroma in man, the lipoid deposits play an important part in subsequent development of the arterial lesions. Discussion of Winternitz's studies on the etiology of atheroma concludes with the statement: "It seems doubtful that intimal hemorrhages can be regarded as an etiologic factor in the production of atheroma." Under pneumoconiosis it is pointed out that "in pure anthracosis there is never marked fibrosis." Where marked fibrosis occurs in anthracosis, silicosis also is almost always present. An excellent summary deals with the increased frequency of bronchogenic carcinoma ("primary carcinoma of the lung"). Boyd believes that the increased frequency is apparent rather than real. The discussion of jaundice is masterly. The section on diseases of the adrenal glands has been rewritten and in it are included the modern concepts of adrenal insufficiency and the possible role of the cortex in sex determination.

This book should be consulted by all internists, practitioners, pediatricians, pathologists and medical students. The surgeons will also find in it a source of valuable information.

The Diagnosis and Treatment of Pulmonary Tuberculosis. By John B. Hawes, 2d, M.D., Late President of the Boston Tuberculosis Association; and Moses J. Stone, M.D., Assistant Professor of Medicine, Boston University, School of Medicine. Second Edition. 260 pages, illustrated. Philadelphia: Lea & Febiger, 1940. Cloth, $2.75.

This book on pulmonary tuberculosis represents the rich experience of many years of tuberculosis practice by two recognized authorities. It is eminently practical and thoroughly covers modern methods of diagnosis and treatment. Most pathologists will warm to this work because it clearly stresses the essential facts useful in practice.

Tuberculosis of Bone and Joint. By G. R. Girdlestone, M.A., B.M., Oxon., F.A.C.S., Eng., Nuffield Professor of Orthopedic Surgery, New College, Oxford. 265 pages, illustrated. New York: Oxford University Press, 1940. Cloth $8.75.

This is one of the best volumes of its type that has been written. It has demanded great study and care and comes from an orthopedic surgeon who has had a wide experience in such disabilities. The author states that he lost a middle finger several years ago on account of a tuberculous infection contracted from a tuberculous patient.

According to the author, tubercle bacilli are carried to the spot by the blood, probably with the debris breaking down from lymph nodes. In children the occurrence of various embolic lesions close to the joints or epiphyseal disks, whether tuberculous, pyogenic, or due to uninfected infarction, is relatively common. This is caused by lack of arterial anastomosis in these regions, where small areas of bone lie beside, or are surrounded by avascular cartilage. The author suggests that in young children a clinical diagnosis, carefully tested and reviewed, is all that is needed. In children, persistence of a chronic decalcifying arthritis is sufficient for all practical purposes. A diagnostic operation is indicated only when a diagnosis cannot be reached by other means. In children, exact diagnosis is rarely urgent and the author states that arthrotomy is indicated only when the patient is ready in the stage as well as in the age for fusion. At an early stage the removal of an enlarged regional lymph node is preferable.

The author outlines the general treatment of bone tuberculosis. The general treatment is rest, food, sunlight and open air.

Girdlestone has very capably presented in regional form the treatment of tuberculosis in different joints. The spine and knee joint chapters are the most outstanding.

This is one of the many contributions given to orthopedic surgery by the British orthopedic profession. One wonders how many more there will be and in the present crisis one wonders where this author is and what hardships and worries have assailed him.

Orthopedic Operations: Indications, Technic and End Results. By Arthur Steindler, M.D., F.A.C.S., Professor of Orthopedic Surgery, the State University of Iowa, Iowa City, Iowa. 766 pages, illustrated. Springfield, Illinois: Charles C. Thomas, 1940. Cloth $9.00.

This is a comprehensive book based on the writer's vast personal experience. The author points out the limitations of such a book of observations, but justifies his work by the statement that "personal conviction backed both by reflection and by experience is the mainspring of unbiased teaching." He acknowledges that many commonly accepted operative procedures are omitted because "their validity did not impress itself sufficiently, or they represented merely irrelevant variations of a general principle."

The book is divided into three parts. The first concerns itself with general surgical facts and with the general approaches to operations. The second part gives various operative procedures on the several structures of the locomotor system. The third presents the precise clinical situations in which these operations are to be applied. The procedures are adequately discussed as to indications, technic and end results.

The illustrations are adequate and the reference lists very complete. In addition to its valuable content, this book has a very attractive physical appearance. The print is large and clear on beautiful gloss paper and the binding is artistic as well as durable.

Otolaryngology in General Practice. By Lyman G. Richards, M.D., Assistant in Surgery, Harvard Medical School and Associate Professor of Otolaryngology, Tufts Medical School, Boston, Massachusetts. With a Foreword by D. Harold Walker, M.D., Professor Emeritus of Otology at Harvard Medical School, Past President of American Otological Society, Former Chief and Present Consultant in Otology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts. 352 pages, illustrated. New York: The Macmillan Company, 1939. Cloth $6.00.

This book is written for the practitioner who is interested in otolaryngology from a general viewpoint. The great majority of operative procedures in this

field are held for the specialist, but the operation for tonsillectomy and adenoidectomy is described in detail and with vivid clearness. A few other minor operations are suggested as being capable of performance by the average physician. Attention is given to methods of examination and the treating of the common disorders which often come into the hands of the busy practitioner. The author is perhaps ultra-conservative in his delegation of a portion of this field to the general physician. However, there is a great deal to learn from this text.

Medical Entomology: With Special Reference to the Health and Well-Being of Man and Animals. By William B. Herms, Professor of Parasitology in the University of California, Consulting Entomologist for the California State Board of Health, Honorary Member National Malaria Committee. Third Edition. 582 pages, illustrated. New York: The Macmillan Company, 1939. Cloth $5.50.

Due to the many advances made in the past few years, Dr. Herms has completely revised his book. Arachnids, cockroaches, beetles, bugs, lice, gnats, mosquitoes, horseflies, snipe flies, houseflies, fleas, ticks, mites and arthropods are discussed in full detail. The chapters on mosquitoes and ticks are especially noteworthy, as the writer is an international authority on these subjects. The importance of these insects as vectors in human and animal disease from a public health standpoint is emphasized. The book is of value to the sanitary engineer in the study of the habits of these insects and their abatement by methods at his disposal, all of which are given. The bibliography is very extensive.

Southern Medical News

ALABAMA

Dr. Gilbert F. Douglas, Birmingham, was re-elected Chairman of the Council of the Chattahoochee Valley Medical Association at the recent annual meeting in Atlanta. The Association will meet in Jacksonville, Florida, next year.

Dr. Louise Branscomb, Birmingham, was recently the principal speaker at the Twelfth Annual Founders' Day Banquet of the Howard College Chapter of Alpha Epsilon Delta, national honorary pre-medical fraternity.

Deaths

Dr. Charles David Mason, Eutaw, aged 53, died May 17 of injuries received in an automobile accident.

ARKANSAS

The Ninth Councilor District Medical Society has elected the following officers for the coming year: President, Dr. Ross Fowler, Harrison; Vice-President, Dr. D. K. McCurry, Green Forest; Secretary-Treasurer, Dr. J. G. Gladden, Harrison.

Dr. W. A. Snodgrass, Jr., Pine Bluff, took special work at the State Sanatorium during May.

Dr. R. H. Ray, Earle, has erected a new office building.

Dr. Dewell Gann, Sr., Benton, has been elected Treasurer of the Benton Chapter of Royal Arch Masons.

Dr. S. C. Fulmer and Dr. H. A. Higgins, both of Little Rock, have been appointed heads, respectively, of the Department of Medicine and Department of Surgery of the University of Arkansas School of Medicine.

Dr. H. King Wade, Hot Springs National Park, has been elected a Director of the Chamber of Commerce of that city.

Dr. Frank Vinsonhaler, Little Rock, gave the memorial address for the Military Order of the World War on May 26.

Dr. S. A. Thompson, Camden, has been elected a Director of the Lions Club of his city.

The Alumni of the University of Arkansas School of Medicine have elected the following officers for the coming year: President, Dr. Fount Richardson, Fayetteville; Vice-President, Dr. G. W. Reagan, Little Rock; Secretary-Treasurer, Dr. T. Duel Brown, Little Rock.

Dr. J. B. Elders has removed from Walnut Ridge to Harrisburg.

Dr. A. C. Shipp, Little Rock, attended the National Tuberculosis Association meeting in Cleveland as Director from Arkansas.

Staff appointments announced at the University Hospital, Little Rock, are: Medicine, Dr. S. C. Fulmer, Chief, Dr. Doyle Fulmer, Dr. D. T. Hyatt, Dr. C. Lewis Hyatt, Dr. R. E. McLochlin, Dr. F. W. Harris, Dr. Alan G. Cazort and Dr. H. A. Dishonah; Surgery, Dr. H. A. Higgins, Chief, Dr. George V. Lewis, Dr. C. C. Reed, Jr., Dr. R. T. Smith, Dr. D. R. Hardeman, Dr. H. G. Hollenberg, Dr. J. K. Donaldson, Dr. Harry Hayes, Dr. Robert Caldwell, Dr. F. Walter Carruthers and Dr. H. Fay H. Jones.

Dr. N. T. Hollis, Little Rock, has been elected to membership in the American Psychiatric Association.

Dr. W. F. Shearer, Little Rock, has been appointed city physician.

Dr. R. M. Jernigan, Jonesboro, took special work in proctology in New Orleans recently.

Deaths

Dr. Raymond T. Smith, Fort Smith, aged 46, died June 2 of injuries received in an automobile accident.

Dr. Wayne Neal Freemyer, Little Rock, aged 56, died May 30.

Dr. Felix M. Williams, Hot Springs National Park, aged 78, died April 11 of a streptococcic infection of the throat.

Dr. William Lee Patterson, El Dorado, aged 60, died May 30.

Dr. William T. McDonald, Vilonia, aged 74, died May 26 of chronic myocarditis and nephritis.

DISTRICT OF COLUMBIA

Dr. William Thornwall Davis and Dr. Tomas Cajigas, both of Washington, recently received the decoration of the Order of Carlos J. Finley at a reception given at the Cuban Embassy by the Ambassador, Dr. Pedro Martinez Fraga. The presentation was made by Dr. Juan M. Moya, Secretary of Sanitation of Cuba, in the presence of diplomats from twenty-one American republics as well as delegates to the Eighth American Scientific Congress.

Several new committees of the Medical Society of the District of Columbia have been created recently and changes in personnel have occurred in others. Obituary Committee—Dr. Thomas S. Lee, Chairman; Dr. Stuart O. Foster, Dr. Frank M. Hand, Dr. Edward Lewis and Dr. Richard J. McNulty. Committee on Relations with the Legal Profession—Dr. Don Johnson, Chairman; Dr. Linn F. Cooper and Dr. Russell K. Hollingsworth. Committee on Relations with the Dental and Pharmaceutical Professions—Dr. Lyman B. Tibbets, Chairman; Dr. Thomas Bradley and Dr. Edward B. Kelly. Additions to the Medical Bureau Committee are: Dr. Norvell Belt, Dr. William F. Burdick, Dr. Allen S. Cross and Dr. Herman S. Hoffman.

Dr. Ruth Jackson, Washington, will represent the Society on a joint Civil Service Committee with the District of Columbia Chapter of the American Institute of Chemists and other local organizations.

The George Washington University Medical Society has elected the following officers for the coming year: President, Dr. William B. King; President-Elect, Dr. Howard F. Kane; First Vice-President, Dr. J. Burton Glenn; Second Vice-President, Dr. Katharine A. Chapman; Secretary-Treasurer, Dr. Leslie H. French, all of Washington.

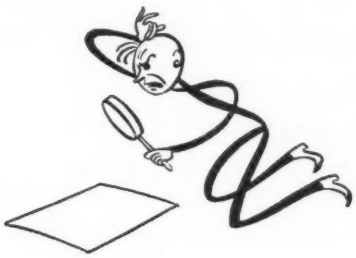
The Jacobi Society has elected the following officers for the coming year: President, Dr. Isadore Rodis; Vice-President, Dr. Samuel M. Dodek; Secretary, Dr. Joseph Dessoff; Treasurer, Dr. Joel N. Novick.

The following physicians have been elected to the Board of Directors of the Social Hygiene Society for the 1940-43 term: Dr. Edith SeVille Coale, Dr. Lewis C. Ecker, Dr. Robert S. Lamb, Dr. William J. Mallory and Dr. Daniel Seckinger.

Dr. William P. Herbst represented the American Urological Association and Dr. Wallace M. Yater represented the American Society for Clinical Investigation at the recent Eighth American Scientific Congress held in Washington.

The 1940-41 Edition of Who's Who in America includes among its new names the following members of the Medical Society of

Continued on page 34



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Continued from page 910

the District of Columbia: Dr. William DeKleine, Dr. Robert Oden, Dr. Ivay A. Pelzman, Dr. Norman P. Scala and Dr. Sara E. Branham.

Dr. J. Winthrop Peabody, President of the District of Columbia Tuberculosis Association, made one of the welcoming addresses at the Second Annual Conference of Negro Tuberculosis Workers recently held in Washington.

DEATHS

Dr. Alexander S. Barger, Washington, aged 74, died May 1 of arteriosclerosis and hypertension.

FLORIDA

Dr. R. B. McIver, Jacksonville, was elected Secretary of the Chattahoochee Valley Medical Association at the recent annual meeting in Atlanta. The Association will meet next year in Jacksonville.

The Florida Railway Surgeons' Association elected the following officers for the coming year: President, Dr. Leland F. Carlton, Tampa; President-Elect, Dr. J. W. Alsobrook, Plant City; Vice-President, Dr. Z. Brantley, Grandin; Secretary-Treasurer, Dr. Walter C. Page, Cocoa.

The Florida Association of Industrial Surgeons has elected the following officers for the coming year: President, Dr. A. M. Bidwell, Tampa; President-Elect, Dr. G. F. Oetjen, Jacksonville; Vice-President, Dr. Kenneth A. Morris, Jacksonville; Secretary-Treasurer, Dr. T. H. Roberts, Lakeland.

The Florida Radiological Society has elected the following officers for the coming year: President, Dr. Joseph H. Lucinian, Miami; Vice-President, Dr. John N. Moore, Ocala; Secretary-Treasurer, Dr. Elliott M. Hendricks, Fort Lauderdale.

Dr. Frederick Oetjen, Jacksonville, attended a Postgraduate Course in Industrial Medicine during the month of May given by the American College of Physicians at the Henry Ford Hospital, Detroit, Michigan.

Dr. J. R. Nieder, Delray Beach, is taking a six weeks' intensive course in Medicine given at Harvard University.

DEATHS

Dr. William A. Chapman, Miami, aged 53, died April 30 of septicemia following abscess of the right hip joint due to an automobile accident.

Dr. Reuben Baston Dearborn, Miami Beach, aged 59, died April 17.

Dr. Henry B. Stanley, Gainesville, aged 73, died April 8.

Dr. Laura Ewing Reading, Tampa, aged 89, died May 12 of chronic myocarditis.

GEORGIA

Dr. Frank K. Boland, Atlanta, was elected President of the Chattahoochee Valley Medical Association at the recent annual meeting in Atlanta. Dr. Boland has been Secretary for the past five years. The Association will meet next year in Jacksonville, Florida.

Dr. A. K. Swift and Dr. J. O. Simmons, both of Woodbine, formally opened their new hospital at Woodbine recently.

Dr. J. Allen Smith, Macon, recently completed a postgraduate course under Dr. Chevalier Jackson at Temple University School of Medicine, Philadelphia, Pennsylvania, in peroral endoscopy and announces the opening of a Bronchoscopic Department at the Macon City Hospital.

Dr. Stephen T. Brown, Atlanta, announces the association of Dr. S. Ross Brown in the practice of urology and urological surgery.

The Children's Ward of the Macon Hospital, Macon, which was recently completed, has been named and dedicated in honor of Dr. Olin H. Weaver, who is now Chief of Staff of the entire hospital and has been continuously connected with its management since its opening in 1895.

Dr. William R. Camp, Fairburn, recently celebrated his fiftieth year in the practice of medicine.

Dr. Robert E. Adair, Cartersville, recently celebrated his fiftieth year in the practice of medicine.

The Georgia Public Health Association held its annual meeting at the Ansley Hotel, Atlanta, under the presidency of Dr. William H. Weir, Atlanta. Dr. John R. Evans, Decatur, Health

Continued on page 36

Diarrhea in Infancy

Take It In Time

Just a day or two of light nourishment prepared from Mellin's Food as suggested below will usually avert an intestinal disturbance that might develop into a serious diarrhea if not taken in hand at the first appearance of loose stools.

Mellin's Food*. . 4 level tablespoonfuls

Water (boiled, then cooled) . . . 16 ounces

Give one to three ounces every hour or two until the stools lessen in number and improve in character.

The mixture may then be strengthened by the gradual substitution of boiled skimmed milk for water until the quantity of skimmed milk is equal to the normal quantity of milk used in the baby's formula. Finally the fat of the milk may be gradually replaced by skimming less and less cream from the milk.

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Continued from page 34

Commissioner of DeKalb County, was elected President of the Association.

The following physicians are members of the State Board of Health: Dr. Claude Griffin, Atlanta, President; Dr. Harold P. McDonald, Atlanta, Vice-President; Dr. H. G. Huey, Homerville; Dr. R. F. Wheat, Bainbridge; Dr. Steve P. Kenyon, Dawson; Dr. O. B. Walker, Bowman; Dr. J. W. Palmer, Ailey; Dr. G. T. Lyon, Roswell; Dr. L. G. Neal, Cleveland; and Dr. J. B. Warnell, Cairo.

Dr. J. Zeb McDaniel and Miss Opal Lois Dowden, both of Augusta, were married April 13.

DEATHS

Dr. Vasco Mortimer Beecher, Jr., Atlanta, aged 25, died May 21 of injuries received in an automobile accident.

Dr. Joseph Walter Rogers, Macon, aged 82, died May 1 of chronic cystitis.

Dr. Clarence Ernest Pickett, Richland, aged 70, died April 26.

Dr. Albert W. Lewis, Jr., Atlanta, aged 29, died May 13.

Dr. Benjamin F. Shamblin, Lyerly, aged 81, died May 20.

Dr. George T. Ridgway, Royston, aged 69, died May 12.

KENTUCKY

The Kentucky State Medical Association will hold its annual meeting in Lexington, September 16-19. Dr. A. T. McCormack, Louisville, is Secretary.

On June 12, 1940, the Kentucky Prenatal Law became effective.

Dr. Virgil E. Simpson, Louisville, who has represented the Kentucky State Medical Association for the past twenty years on the Committee on the Revision of Pharmacopoeia, attended the recent meeting of the Committee held in Washington. The Pharmacopoeil Revision Committee is a distinctly scientific organization and it is an honor for Kentucky to have one of its active members.

Continued on page 38

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A combined surgical course comprising General Surgery, Traumatic Surgery, Abdominal Surgery, Gastro-Enterology, Proctology, Gynecological Surgery, Urological Surgery, Thoracic Surgery, Pathology, Roentgenology, Physical Therapy, Operative Surgery and Operative Gynecology on the Cadaver.

Obstetrics and Gynecology

A full time course. In Obstetrics: Lectures; prenatal clinics; witnessing normal and operative deliveries; operative obstetrics (manikin). In Gynecology: Lectures; touch clinics; witnessing operations; examination of patients pre-operatively; follow-up in wards post-operatively. Obstetrical and Gynecological pathology; regional anesthesia (cadaver). Attendance at conferences in Obstetrics and Gynecology. Operative Gynecology on the Cadaver.

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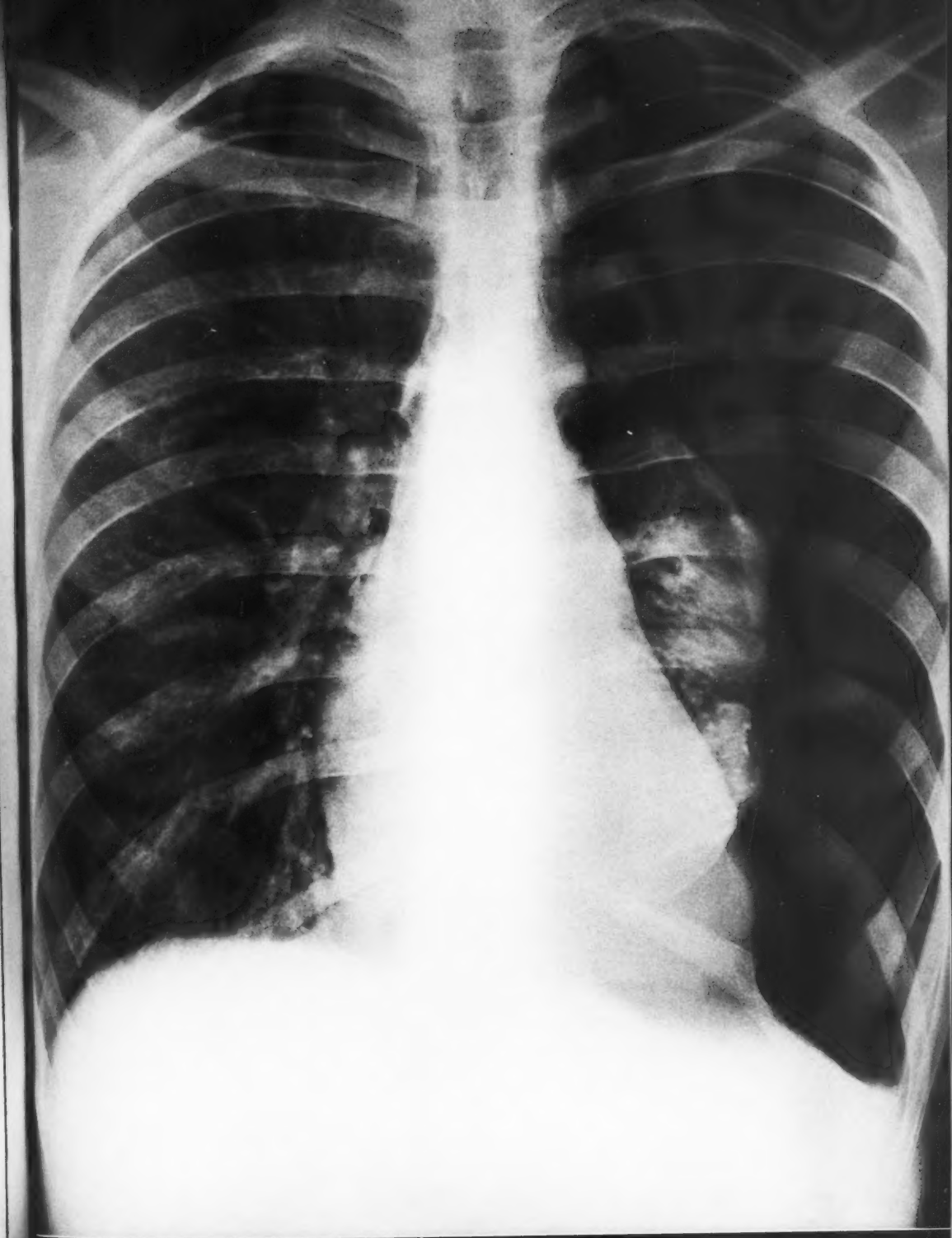

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BLUE *BRAND EASTMAN ULTRA-SPEED SAFETY X-RAY FILM*

(*See back of this page*)

Excerpts from the Medical Literature....

"The better understanding of the nature of pulmonary tuberculosis and the ability to visualize the lesions and what may happen to them under treatment, made possible by roentgenology, have allowed the use of collapse therapy. Indeed, the roentgen ray has made collapse therapy possible and, instead of the cavity being the death knell of its bearer, many are saved by prompt application of one or more of the collapse measures available."

—Am. J. Roentgenol., *30:* 307, September, 1933

"Before operative intervention [in conditions of pulmonary tuberculosis] is decided on, a review of the history and a careful, complete examination of the patient should be made; a meticulous study of the evolution and the present status of the lesions in the lung, so graphically and chronologically recorded by a series of x-ray films, is imperative."

—J.A.M.A., *112:* 138, January 14, 1939

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Continued from page 36

The May meeting of the Johnson County Medical Society at Paintsville was held in the form of a Pediatric Clinic in charge of Dr. Philip F. Barbour, Louisville, assisted by Dr. Oma Creech, Louisville; Dr. W. T. Maxson and Dr. A. J. Alexander, Lexington; Dr. A. D. Sloan, Dr. Lon C. Hall, Dr. L. B. Sheppard, Dr. H. G. Skaggs, Dr. G. P. Salyers, of Paintsville, and the Johnson County Health Department nurses. Forty-six children passed through the Clinic and many interesting cases were seen.

Dr. C. C. Howard, Glasgow, recently addressed the Rotary Club in Bowling Green, showing pictures made in France of the American Expeditionary Forces during the World War.

DEATHS

Dr. Edgar Duff Burnett, Anchorage, aged 61, died April 7.

Dr. John Glover South, Louisville, aged 67, died May 13.

Dr. Caleb A. Calvert, Scottsville, aged 63, died May 26 of cerebral hemorrhage and arteriosclerosis.

Dr. John William Hayes, Franklin, aged 75, died April 10.

Dr. Richard Allen, Winchester, aged 81, died May 30 of cerebral hemorrhage.

LOUISIANA

The New Orleans Graduate Medical Assembly has elected the following officers for the coming year: President, Dr. Val H. Fuchs; First Vice-President, Dr. F. E. LeJeune; Second Vice-President, Dr. D. J. Murphy; Third Vice-President, Dr. D. N. Silverman; Treasurer, Dr. W. H. Gillentine; Secretary, Dr. J. S. D'Antoni.

Dr. W. H. Perkins, New Orleans, presided over the Baby Health Bill meeting recently held in New Orleans. Addresses were delivered by Dr. Walter Levy and Dr. Eugene B. Vickery.

Dr. A. E. Fossier, New Orleans, was recently elected to honorary membership in the History of Medicine Society of the Tulane University of Louisiana School of Medicine.

Dr. Val H. Fuchs, New Orleans, has been elected to membership in the American Laryngological Society.

Continued on page 40

Prevent Infection

Outdoor activities at this season cause many minor injuries for which physicians require an antiseptic.

MERCUROCHROME, H. W. & D., satisfies your antiseptic requirements. Tablets or powder provide convenient means of preparing stock solutions. Solutions do not deteriorate, providing for economy in use.

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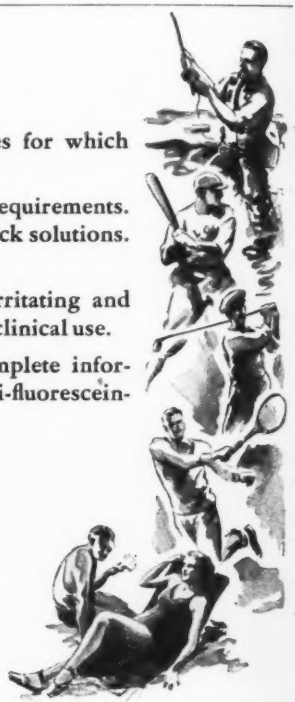

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Continued from page 38

Dr. Ernest Carroll Faust, Professor of Parasitology, Department of Tropical Medicine, Tulane University of Louisiana, New Orleans, has been made an honorary member in the Eugene Field Society, a national association of authors and journalists, in recognition of the literary skill and craftsmanship of his works.

Dr. Woodard Davis Beacham, New Orleans, announces the opening of offices at 1110 Pere Marquette Building for the practice of gynecology, obstetrics and female urology.

DEATHS

Dr. John A. Lanford, New Orleans, aged 59, died July 2.

Dr. Royal Lee Love, De Ridder, aged 62, died March 30.

Dr. Benjamin Franklin Easter, New Orleans, aged 65, died May 16 of bronchopneumonia.

Dr. Wilkins McDade, Minden, aged 54, died May 24 of injuries received in an automobile accident.

Dr. Pete Ernest Magoun, Vidalia, aged 56, died April 8.

Dr. Foster Thomas Jones, New Orleans, aged 50, died May 28 of cerebral hemorrhage.

Dr. John Luther Pittman, Palmetto, aged 72, died April 19.

Dr. Arthur Joseph Babin, New Orleans, aged 66, died May 19 of chronic nephritis and cirrhosis of the liver.

MARYLAND

Dr. Guy L. Hunner, Professor of Gynecology, Johns Hopkins University School of Medicine, Baltimore, was recently honored when the workers of his department presented a portrait of him to the University. Mrs. John Parsons, Dr. Hunner's daughter, painted the portrait.

The Twentieth Annual Conference of the Field and Departmental Staffs of the Maryland State Department of Health was recently held in Baltimore. A distinguished group of speakers furnished an instructive program.

The new hospital unit at the District Training School in Laurel was dedicated recently. Among the speakers at the dedicatory ceremonies were Mrs. Franklin D. Roosevelt, Dr. James Lewald, Superintendent, and Dr. Winfred Overholser, Superintendent of St. Elizabeth's Hospital.

Dr. Benjamin Owen Ravenel, Baltimore, and Miss Evelyn Martion of Columbia, South Carolina, were married May 24.

DEATHS

Dr. Ernest Rowland, Liberty Grove, aged 65, died April 27 of chronic myocarditis and nephritis.

MISSISSIPPI

Dr. Ralph Sneed, University, has been named Director of the newly organized Health Department of Marion County.

Dr. Alton R. Perry, Laurel, has resigned as Director of the Jones County Health Unit, a position he has held since the department was established three years ago.

Dr. Ransom J. Jones, Poplarville, has been appointed Director of the Leflore County Health Department. Dr. Edwin H. West, Purvis, will succeed Dr. Jones as Director of the Southeastern Health District.

Dr. Byron O. Garner, Greenwood, has been made full time Director of Noxubee County.

Dr. James H. White, Corinth, has been placed on a full time basis as Health Officer in Alcorn County.

Dr. Lynn D. Abernethy, Grenada, has been made Director of Health in Marshall County, relieving Dr. John W. Dugger, who has been acting Health Officer since the resignation of Dr. John W. Dorman.

Dr. Murphy M. Sims, Lexington, has been appointed Health Officer of Lafayette County, succeeding Dr. James H. Armstrong, Oxford, who resigned to enter private practice.

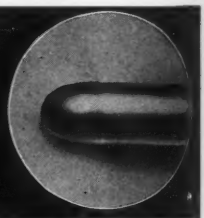
DEATHS

Dr. William Robert Gilbert, Tyro, aged 61, died April 5.

Dr. Alphonse Ames Kergosien, Bay St. Louis, aged 59, died April 23 of chronic encephalitis.

Continued on page 44

RADON SEEDS



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And Then

Another outstanding thing has been done. It has been demonstrated that when a product is supplied at a price which people of low incomes can pay, supplied through the wholesaler and retailer and then all treatment directed to the neighborhood physician and health department, a fatal scourge, even during the depression, through the private practitioner, is being conquered.

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We are as sorry as anyone about this unit business. The International Unit, by definition, refers to estrone, the excretory form of the female sex hormone and was established before ∝-estradiol was discovered. It is not applicable to ∝-estradiol which is the "primary or true ovarian hormone produced in the follicle"[1] and "the most effective of natural estrogens."[2] PROGYNON-B and PROGYNON-DH† being forms of ∝-estradiol, are labelled in Rat Units.

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*One ampule of 2000 R. U. PROGYNON-B† is equivalent in effect to 10 ampules of 2000 I. U. estrone (theelin).

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SCHERING

SCHERING CORPORATION • BLOOMFIELD, NEW JERSEY

Continued from page 40

MISSOURI

Dr. Owen W. Krueger, Kansas City, was recently honored at a dinner at St. Margaret's Hospital in celebration of his fiftieth year in the practice of medicine.

The Ellis Fischel State Cancer Hospital at Columbia has elected the following officers: Chief of the Consultant Staff, Dr. Dudley A. Robnett, Columbia; Vice-Chief of Staff, Dr. Alphone McMahon, St. Louis; Secretary, Dr. E. Kip Robinson, Kansas City; Members of the Executive Committee, Dr. James R. McVay, Kansas City; and Dr. Louis H. Jorstad, St. Louis.

Dr. Hal Foster, Kansas City, recently received the first award of the Kansas City Society of Ophthalmology and Otolaryngology, in recognition of his organization of the American Academy of Ophthalmology and Otolaryngology and the Kansas City Society of Ophthalmology and Otolaryngology.

Dr. Thomas Findley, Jr., St. Louis, and Miss Jean Kyer, Ann Arbor, Michigan, were married in St. Louis on April 11.

DEATHS

Dr. C. H. McCaslin, Kansas City, aged 87, died April 29 of arteriosclerosis and hypertension.

Dr. William Thomas Coughlin, St. Louis, aged 67, died May 22.

Dr. Joseph F. Flynt, Paris, aged 71, died May 3 of pneumonia.

Dr. Fred Elliott Hobbs, St. Louis, aged 66, died May 12 of heart disease.

Dr. Herman Albert Hanser, St. Louis, aged 62, died May 28 of heart disease.

Dr. Richard Kring, St. Louis, aged 76, died May 16 of chronic myocarditis and arteriosclerosis.

Dr. Preston Thompson, Lebanon, aged 51, died April 14.

Dr. George Frederick Sneed, Kirksville, aged 47, died May 10 following an operation for a brain tumor.

Dr. Riley F. Cheatham, Diamond, aged 70, died April 3 of carcinoma of the prostate.

Dr. John D. Ball, Lexington, aged 80, died May 23 of ascending pyelonephritis.

Dr. Jacob Hall, Kansas City, aged 81, died May 7 of cerebral hemorrhage.

NORTH CAROLINA

Dr. Paul P. McCain, Sanatorium, was elected President of the National Tuberculosis Association at the recent June meeting in Cleveland.

Dr. W. C. George, Chapel Hill, has been made Head of the Department of Anatomy, University of North Carolina Medical School, succeeding the late Dr. C. S. Mangum.

Dr. Wm. deB. MacNider, Chapel Hill, has resigned as Dean of the Medical School in order to devote his time to research and teaching.

Duke University, Durham, announces the establishment of the Charles W. Hargitt Research Fellowship in Zoology. The fellowship was made possible by a bequest in the will of the late Charles Wesley Hargitt, Ph.D., for many years Research Professor of Zoology at Syracuse University. Dr. Hargitt's son, George T. Hargitt, Ph.D., is Professor of Zoology at Duke. It is expected that the fellowship will be granted in 1941 for research in cytology.

Dr. Archie A. Barron, Charlotte, announces the opening of a Neuropsychiatric Institute for the diagnostic study and interpretation of nervous symptoms.

Dr. Thomas H. Byrnes, formerly pathologist to Watts Hospital in Durham, announces his association with Dr. Lester C. Todd in the practice of pathology and allergy in Charlotte.

Dr. Ralph Moschella and Miss Helen Holmesley, both of Statesville, were married April 8.

DEATHS

Dr. Benjamin Thomas Atkins, Shallotte, aged 62, died May 9 of urinary extravasation with gangrene and urethral stricture.

Dr. Arthur Eugene Knoefel, Sr., Black Mountain, aged 67, died May 20 of coronary occlusion.

Dr. William Canova Peterson, Jr., Wilmington, aged 49, died April 10.

Continued on page 46

MOTHER WAS A DRYCO BABY, TOO

THINK BACK FOR A MOMENT, doctor. How many infant foods and feeding fads have you seen come and go since Dryco was introduced more than twenty years ago?

A great number, of course. But *one* has staunchly ridden the storms of conflicting medical opinion through that turbulent period. Today, Dryco, the pioneer, occupies a position of trust that is a tribute to its integrity and the soundness of the convictions which led to the development of this moderate-fat, high-protein infant food, over twenty years ago.

The Dryco of today, though basically unchanged, has pioneered in the improved packing methods which insure keeping qualities, is irradiated to provide the antirachitic protection of Vitamin D.

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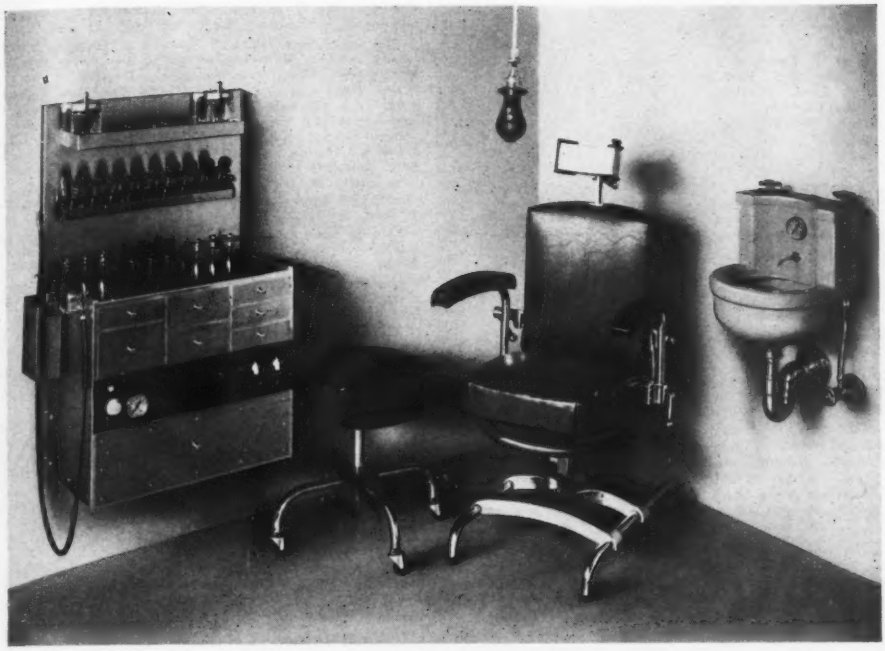

AN E.N.T. TREATMENT ROOM IN A SMALL AREA

The dimensions in the above photograph are 5′ 9″ along one wall and 4′ 2″ along the other. In this area, conveniently arranged, is everything needed to make a complete ear, nose and throat examination. The complete absence of piping and wiring is especially noticeable. We wish to call attention to the new cuspidor which is now combined with the suction.

Treatment Cabinet: Covered with stainless steel, with casting of a non-corroding aluminum alloy. Contains: air regulator with gauge, tubing, cutoff and air filter; nasopharyngoscope rheostat; push button; cautery transformer and rheostat; transilluminator complete with rheostat, cord, handle, lamps, antrum and frontal tips; seven metal drawers on fiber runners and one large drawer for towels; waste container; bakelite covered work table; space for six spray bottles, twelve solution bottles, shelf for cotton jars; pocket for history card or prescription blanks; and a spray bottle heater; the whole presents an attractive appearance and will not tarnish and is easy to keep clean. $125.00. Can be furnished without air or electrical equipment for $75.00. (Glassware not included.)

Chair: Can be placed in horizontal position, will not tip in this position; raised and lowered by large hand wheel; paper covered headrest removable; locked with foot-pedal; bakelite armrests removable. Removable footrest and handle and chair can be used as a modified turning chair; back locks rigidly in any position. As shown in brown, $75.00.

Combined Suction and Cuspidor: This is an entirely new piece of equipment. It was designed to eliminate the cost of installing a separate suction. The apparatus is 12″ wide and projects 13¼″ from the wall. The flushing rim and the suction is furnished with a vacuum breaker and should meet all plumbing requirements. Complete with trap and valves in green and ivory. $59.50. Extra charge for other colors. Original cuspidor is still being manufactured, being furnished with vacuum breaker. $34.50.

Ceiling Light: A telescopic light attached to the ceiling; for 4 or 5′ lengths (when extended). $10.50. Other lengths available.

Light Shield: Takes an ordinary 60 watt lamp. Will not burst; spot can easily be rotated. $5.00.

Stool: A soft upholstered stool with easy running ball bearing stem casters. $12.50.

Treatment Cabinet for Ophthalmologists: This is similar to the cabinet above except that a thermostatically controlled warming cabinet is included. This cabinet is placed at the level shown for the top shelf. The heater is left on continuously and the setting of the thermostat can be easily changed. This cabinet is slightly higher than that shown in the cut. There is a charge of $25.00 for this addition.

SURGICAL — MECHANICAL — RESEARCH

1901-1903 Beverly Boulevard **Los Angeles, California**

Continued from page 44

OKLAHOMA

Dr. Finis W. Ewing, Muskogee, was chosen President-Elect of the Oklahoma State Medical Association at its recent annual meeting in Tulsa. Dr. Henry H. Turner, Oklahoma City, was installed as President, and Dr. William A. Tolleson, Eufaula, was elected Vice-President.

SOUTH CAROLINA

Dr. T. E. Coleman and Dr. Stanley I. Coleman, Travelers Rest, recently held a reception marking the formal opening of the Coleman private hospital. The hospital is a two-story brick building with a capacity for twenty beds.

The new Kelley Memorial Hospital at Kingstree was recently opened with a dedication service to the memory of the late Lorena Ross Kelley, wife of Dr. E. T. Kelley.

The South Carolina Public Health Association recently held a three-day convention at Myrtle Beach. The following officers were elected for the ensuing year: President, Dr. E. G. McDaniel, Columbia; First Vice-President, Dr. A. W. Humphries, Kershaw; Second Vice-President, Dr. E. T. Ammons, Spartanburg; Secretary-Treasurer, Mrs. Frank George, Columbia.

Dr. Allen H. Johnson formally opened to the public on April 18 the new hospital erected to the memory of the late Dr. L. B. Johnson, his father.

Dr. C. Fred Williams, Columbia, was awarded an honorary degree of Doctorate of Laws by the University of South Carolina during the commencement exercises June 5.

Dr. V. P. Patterson, formerly of Atlanta, Georgia, has opened offices at the Pryor Hospital, Chester, South Carolina, and will take over the hospital connection of Dr. Robert E. Abell.

The Medical College of the State of South Carolina has arranged for a program of instruction in obstetrics and pediatrics for South Carolina physicians. Four physicians will be taken at a time for two weeks of ward rounds and clinics with the college staff. Arrangements are made through the Maternal and Child Health Division of the State Board of Health.

New appointments to the State Board of Medical Examiners include the following physicians: Dr. George C. Brown, Jr., Walterboro; Dr. Wilbur R. Tuten, Fairfax. Drs. Enoch D. Dibble, Marion, and Albert Earle Boozer, Columbia, were reappointed.

Dr. William Morgan Fox, Columbia, has been elected a member of the American Psychiatric Association.

DEATHS

Dr. Theodore James Peake, Clinton, aged 59, died April 14 of peptic ulcer with massive hemorrhage.

Dr. William Joseph Linley, Columbia, aged 69, died May 1 of cerebral hemorrhage.

TENNESSEE

A room to be known as the "Medical Section of the Chattanooga Public Library" is being arranged through a gift of funds and books by the Chattanooga and Hamilton County Medical Society. A collection of approximately one thousand books and bound volumes and a large file of unbound magazines have been given to the Library by the Society as a nucleus of a medical library. Equipment and furniture are being provided by the Library.

The Tennessee Academy of Ophthalmology and Otolaryngology elected the following officers at the recent annual meeting in Chattanooga: President, Dr. William Wesley Wilkerson, Jr., Nashville; Vice-President, Dr. James V. Hodge, Kingsport; Secretary, Dr. William D. Stinson, Memphis, re-elected.

The West Tennessee Medical and Surgical Association recently elected the following officers at the meeting in Jackson: President, Dr. G. W. Brasher, Jackson; First Vice-President, Dr. James Price, Dyersburg; Second Vice-President, Dr. A. T. Hicks, Camden; Secretary, Dr. Geo. R. McSwain, Paris, re-elected; Assistant Secretary, Dr. John Jackson, Dyer.

Continued on page 48

Classified Advertisements

RATES for insertion in the Classified Column are as follows: $2.00 minimum, which includes the first 50 words; for each word in addition to the original 50 words, the charge is 3c.

WANTED, LOCATION FOR SURGEON—Southerner. Protestant. Harvard Medical School graduate. Five years' surgical training. At present, member of surgical staff of Eastern medical school and its hospitals, and first assistant to Head of Surgery Department. Wishes to become associated with surgeon or with group of doctors in the South. Write Dept. B-93, Southern Medical Association, Birmingham, Alabama.

WANTED—Southern location in town having open hospital or will consider location with established man doing surgery, or might consider purchase of small going private hospital. Am American, aged 40, well graduated and trained. Experienced general practice and general surgery. Address Box 163, Wolcottville, Indiana.

MODERN WELL EQUIPPED CLINIC-HOSPITAL for sale, reasonable price. Located on U. S. highway, in a good town of 2,500 inhabitants, near large gas field in Oklahoma; failing health main reason for selling. Dept. S-51, SOUTHERN MEDICAL JOURNAL, Birmingham, Alabama.

Chicago Eye, Ear, Nose & Throat College
Established 1897
231 W. Washington St., Chicago, Ill.

Practical postgraduate course in Ophthalmology and Otolaryngology.

Doctors admitted at any time for review and clinical observation.

Annual Fall Course in Eye Surgery, November 4th to 9th, inclusive. Class limited. Reservations now.

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LaMOTTE BLOOD CHEMISTRY SERVICE

LaMotte Outfit for Determining Sulfanilamide* in Blood and Urine

Developed for use in routine daily examinations. Quantitative result obtained by comparing the treated specimen with standards of known concentration. Only 0.2 c. c. of finger blood and urine are required. Both tests may be completed within 20 minutes. Outfit complete with full instructions, price $22.50 F. O. B. Baltimore, Md.

*May be adapted to sulfapyridine tests also.

This Service includes a series of similar outfits for conducting the following accurate tests: Blood Sugar, Blood Urea, Icterus Index, Phenolsulphonphthalein, Urine pH, Blood pH, Gastric Acidity, Calcium-Phosphorus, Blood Bromides, Blood Proteins, Urinalysis.

LaMotte Chemical Products Co., Dept. S, Towson, Baltimore, Maryland

Wyeth's

SULFUR FOAM APPLICATORS

for the External Application of Sulfur

WYETH'S Sulfur Foam Applicators eliminate the objectionable messiness, smell and discomfort of most sulfur ointments and are acceptable to the patient.

Sulfur Foam is an effective prophylaxis and treatment for scabies and is gaining popularity in other cases where sulfur is indicated externally.

In Sulfur Foam Applicators, the sulfur and a bland soap are impregnated in a special wash cloth. The patient merely moistens the cloth and lathers the area to be treated. The lather dries, leaving a film of sulfur in direct contact with the area.

Wyeth's Sulfur Foam Applicators are supplied in packages of three cloths.

YOU ARE INVITED TO WRITE FOR LITERATURE AND FREE SAMPLES

JOHN WYETH & BROTHER, INCORPORATED
PHILADELPHIA, PA. WALKERVILLE, ONT.

Continued from page 46

The Upper Cumberland Medical Society elected the following officers at the recent meeting held at Cookeville: President, Dr. E. D. Groce, Chestnut Mound; First Vice-President, Dr. V. O. Buttram, Crossville; Second Vice-President, Dr. H. B. Nevins, Livingston; Third Vice-President, Dr. C. C. Howard, Glasgow, Kentucky; Secretary-Treasurer, Dr. L. M. Freeman, Granville.

The Middle Tennessee Medical Society has elected the following officers for the coming year: President, Dr. B. H. Woodward, Spring Hill; Vice-President, Dr. C. H. Hollabaugh, Nashville; Secretary, Dr. R. A. Daniel, Jr., Nashville.

Dr. Jefferson C. Pennington, Nashville, announces the association of Dr. Spencer Johnson, practice limited to urology and urological surgery.

DEATHS

Dr. Henry Erwin Shaw, Ashland City, aged 82, died April 21 of lobar pneumonia and arteriosclerosis.

Dr. James Bowers Bell, Greenville, aged 73, died March 30.

Dr. John N. Wheeler, Chattanooga, aged 68, died April 3.

TEXAS

Dr. Clarence M. Cash, San Benito, was recently honored by a group of women of that city when they dedicated a room in the Valley Baptist Hospital, Harlingen, in his name, in recognition of his professional services during the last forty years. Dr. Cash also received a portfolio of pictures of children whose birth he had attended.

Dr. James E. Peavy, Jr., Austin, has been named Director of the Health Unit for the San Augustine and Sabine Counties.

Dr. Samuel D. Whitten, Greenville, has been appointed Health Officer of Hunt County.

The Tarrant County Medical Society instituted an annual interns' night at its regular meeting on May 22. The program consisted of papers entered in the annual case report contest conducted among residents and interns of the five Fort Worth general hospitals. Dr. Richard G. Scobee was awarded the first prize of $15.00 for his paper entitled "Ectopic Pregnancy." Dr. William D. Sedgwick won second prize of $10.00 for his paper on "Hyperglycemia and Glycosuria in Coronary Thrombosis."

DEATHS

Dr. Elmer Kenneth Umberger, Flatonia, aged 35, died April 23.

Dr. Fred B. Albaugh, Tyler, aged 62, died April 22 of coronary occlusion.

Dr. John W. Thorn, Houston, aged 74, died April 24 of diabetes mellitus.

Dr. Robert Nichols, Houston, aged 59, died May 30 of hyperthyroidism.

Dr. Frederick Richmond Adamson, Abilene, aged 66, died May 28 of coronary occlusion.

Dr. John H. Driver, Brownsville, aged 83, died April 1.

VIRGINIA

The Fourth District Medical Society has elected the following officers for the coming year: President, Dr. W. M. Phipps, Hopewell; Vice-Presidents, Dr. J. B. Kiser, Emporia, and Dr. B. H. Knight, Surry; Secretary-Treasurer, Dr. C. E. Martin, Emporia, re-elected.

Dr. Joseph D. Culbertson, Coeburn, was elected President of the Wise County Medical Society at the recent annual meeting of this Society.

The Norfolk County Medical Society has elected the following officers for the coming year: President, Dr. James W. Anderson; President-Elect, Dr. M. S. Fitchett; Vice-President, Dr. Clayton W. Eley; Secretary-Treasurer, Dr. Lockburn B. Scott, re-elected, all of Norfolk.

Dr. J. H. Hagy, Imboden, was recently elected President of the Clinch Valley Medical Society.

Dr. Clyde F. Ross, Richmond, has been appointed Venereal Disease Control Officer of that city.

Dr. Francis N. Taylor, Petersburg, has been elected Vice-President of the Lions Club of that city.

Dr. B. B. Bagby, Richmond, for the past ten years Director

Continued on page 50

for 27 YEARS this Trade-Mark has been YOUR GUARANTEE of
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QUALITY
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Write for literature containing complete information
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Manufacturers of PURITAN MAID Nitrous Oxid : Cyclopropane : Ethylene : Oxygen Carbon Dioxid : Helium : Mixtures of Carbon Dioxid-Oxygen and Helium-Oxygen. Distributors of leading makes of Anesthetic Gas Machines, Oxygen Tents, Resuscitators, Inhalators, Soda Lime, etc.

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Truly fit "to the Queen's taste" is LORAGA, yet this plain mineral oil emulsion is not disguised by artificial flavoring. There is no oily after-taste. But Loraga not merely caters to the exacting palate of adult or child—it is a fine emulsion that mixes well with the intestinal contents, softens and lubricates the mass so that evacuation may not be delayed and may take place without straining.

Once you use Loraga, you will prescribe it again and again. You will like its trouble-free effectiveness. For an immediate trial, ask for a complimentary supply on your letterhead.

Loraga is available in 16-ounce bottles.

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ALUMINUM ACETATE

Burow's Solution

Rx ALUMINUM ACETATE POWDER (DOAK)

Sig. 1 teaspoonful to a pint of water. Wet dressing as directed.

Therapeutically this prescription is equivalent to 1% Burow's Solution.

Some physicians prefer to add ALUM. ACET. POWDER (DOAK) to milk or a 3% Boric Acid Solution.

The effect of Alum. Acet. (Doak) (Wet Dressing) is antiphlogistic, astringent and antiseptic. Indicated in acute inflammatory skin conditions and moist eczema.

Requests for reprint and sample receive prompt attention. SMJ 8-40

DOAK CO., INC.
CLEVELAND, OHIO

Continued from page 48

of the State Bureau of Maternal and Child Health, has resigned and retired from office.

Dr. M. H. Harris, West Point, has been elected Mayor of that city.

Dr. I. A. Bigger, Richmond, was elected Treasurer of the American Association of Thoracic Surgery at its recent meeting in Cleveland.

Dr. E. Trible Gatewood, Richmond, was recently elected to membership in the American Laryngological Association.

Dr. Richard W. Fowlkes, Richmond, has been elected President of the Alumni Association of Washington and Lee University.

DEATHS

Dr. John Abner Hawkins, Danville, aged 45, died June 7.

Dr. James Morrison, Lynchburg, aged 68, died May 15.

Dr. Donald MacKenzie Faulkner, Richmond, aged 47, died May 6.

Dr. Charles Henry Moncure, Orange, aged 81, died May 11 of uremia.

WEST VIRGINIA

The Wyoming County Medical Society has elected the following officers for the coming year: President, Dr. B. W. Steele; Vice-President, Dr. J. O. Bailiff; Secretary-Treasurer, Dr. J. F. Biggart, all of Mullens.

Dr. John Tallman Jarrett, Dunbar, and Miss Anne Mildred Wood, Richmond, Virginia, were married May 1.

DEATHS

Dr. John Moody Yeager, Marlinton, aged 63, died April 14 of cerebral hemorrhage.

Dr. Karl Steinbeck, Parkersburg, aged 58, died April 20.

Dr. Otis L. Aultz, Charleston, aged 71, died May 14 of arteriosclerosis.

Dr. William Turner Morris, Wheeling, aged 60, died April 30.

Dr. J. D. L. Ball, Milton, aged 89, died May 2 of senility.

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A New Efficient Treatment Room on Convenient Terms

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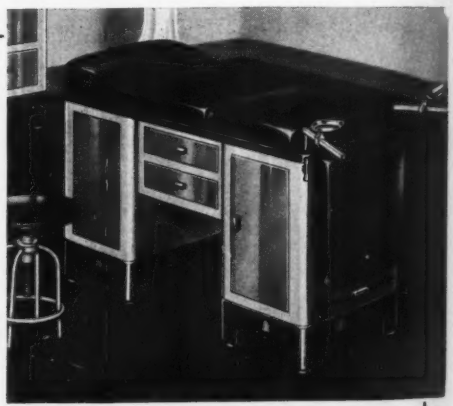

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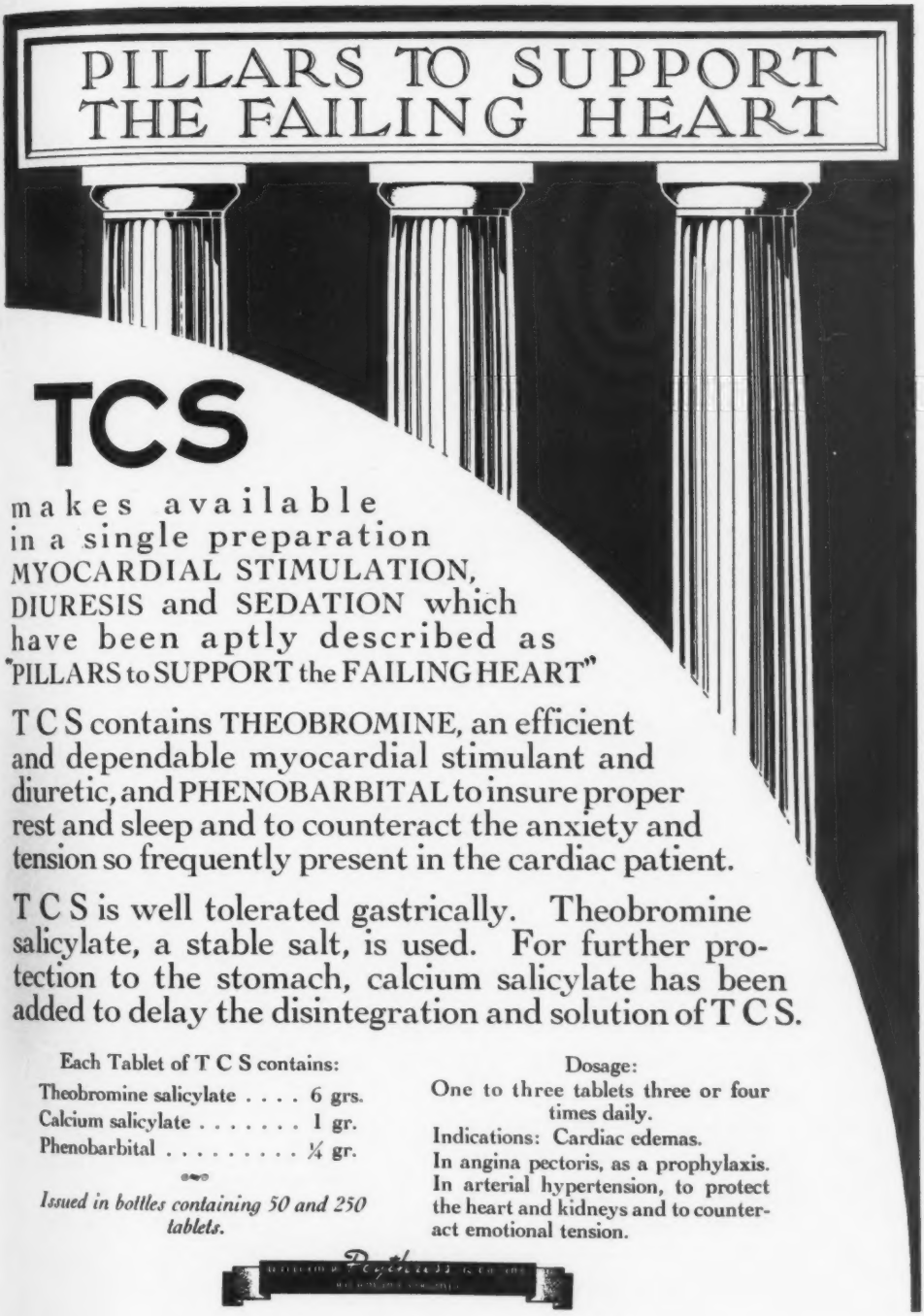

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T C S contains THEOBROMINE, an efficient and dependable myocardial stimulant and diuretic, and PHENOBARBITAL to insure proper rest and sleep and to counteract the anxiety and tension so frequently present in the cardiac patient.

T C S is well tolerated gastrically. Theobromine salicylate, a stable salt, is used. For further protection to the stomach, calcium salicylate has been added to delay the disintegration and solution of T C S.

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Dosage:
One to three tablets three or four times daily.

Indications: Cardiac edemas.
In angina pectoris, as a prophylaxis.
In arterial hypertension, to protect the heart and kidneys and to counteract emotional tension.

Peerless

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VITAMIN B COMPLEX
including nicotinic acid

MEAD'S BREWERS YEAST TABLETS • Each Mead's Brewers Yeast Tablet contains 20 International units of vitamin B_1 (thiamin—the antineuritic factor) and 20 Sherman units of vitamin G (riboflavin). Clinical tests have shown the product to be rich also in nicotinic acid, for the prevention and treatment of pellagra. Supplied in 6-grain tablets in bottles of 250 and 1,000.

MEAD'S BREWERS YEAST POWDER • Each gram (½ teaspoon) supplies 50 International units of vitamin B_1 and 50 Sherman units of vitamin G (the same potency as Mead's Brewers Yeast Tablets), as well as nicotinic acid. Mixes readily with various vehicles the physician may specify in infant feeding. Supplied in 6-oz. bottles.

Mead's Brewers Yeast is nonviable and is vacuum-packed to prevent oxidation. Packed in brown bottles and sealed cartons for greater protection.

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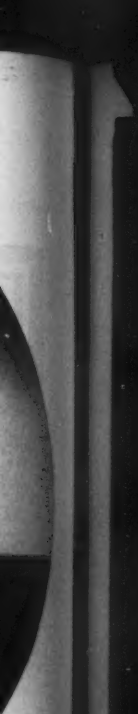

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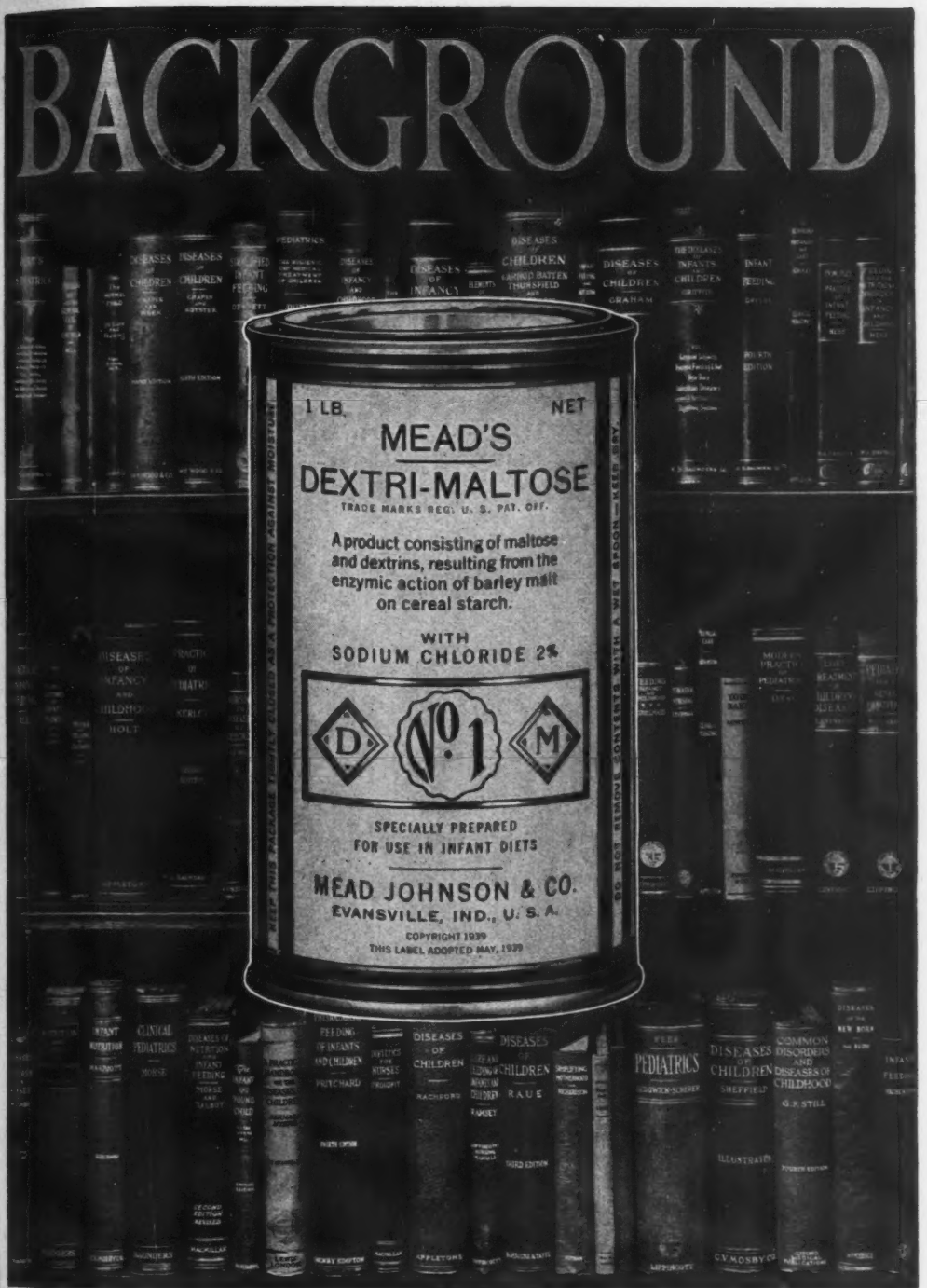
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The young doctor who called on Von Behring

The year—1894. Treatment of diphtheria was largely a matter of topical applications to the throat, and "watchful waiting." Then came the news of von Behring's discovery of diphtheria antitoxin.

Dr. E. M. Houghton, a brilliant new member of the Parke-Davis staff, was promptly sent to Vienna—to learn first-hand from the great scientist the details of diphtheria antitoxin production and use. Soon Parke, Davis & Company established the first commercial biological laboratory in America, and today holds U. S. License No. 1 for the manufacture of biological products for human use.

The courage to pioneer has been characteristic of Parke-Davis since the first years of its existence. In the 1870's came the introduction of cascara. A few years later, the first chemically standardized fluid extracts were introduced. Then, in the '90's came *physiological* standardization. Since the turn of the century, Adrenalin . . . Pituitrin . . . Pitressin and Pitocin . . . Ventriculin . . . Meningococcus Antitoxin . . . Mapharsen.

By broadening and extending its research activities year by year, this Company seeks to fulfill its traditional obligation to the cause of Medicine.

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PIONEERS IN RESEARCH ON MEDICINAL PRODUCTS